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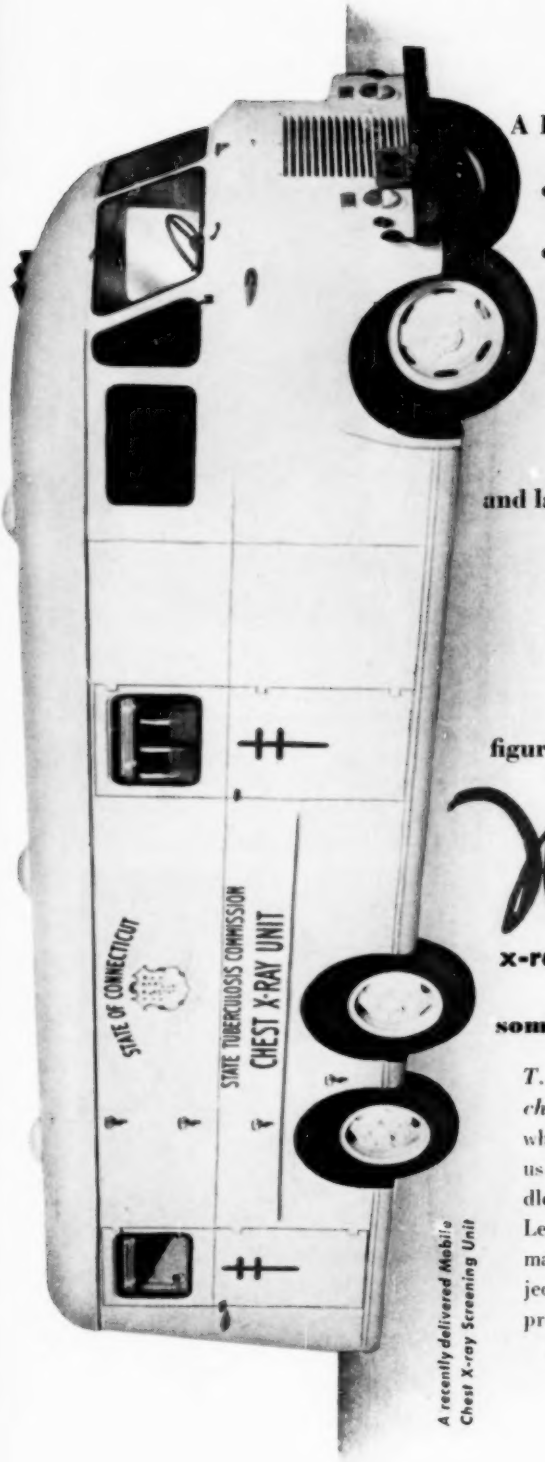

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Barach, A. L., Diseases of the Chest, XII:6:3, 1946

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Cullen, J. H., et al., Diseases of the Chest, XIV:3:345, 1948

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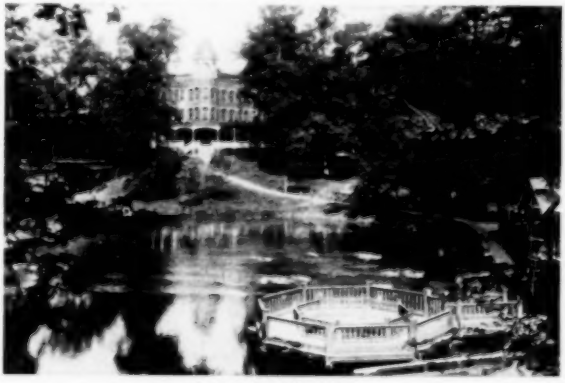

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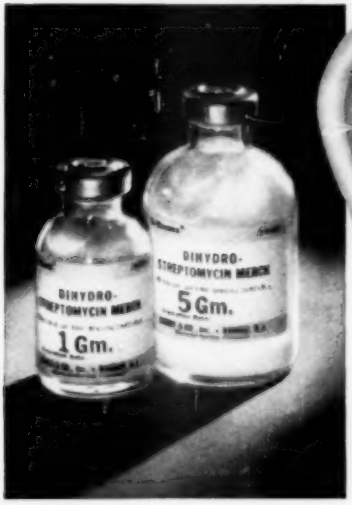

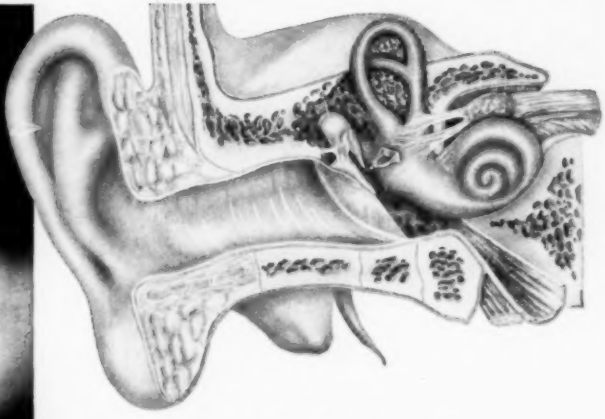

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THE EFFICIENCY OF GAUZE MASKS IN THE PROTECTION OF RABBITS AGAINST THE INHALATION OF DROPLET NUCLEI OF TUBERCLE BACILLI[1, 2, 3]

MAX B. LURIE AND SAMUEL ABRAMSON[4]

INTRODUCTION

Although there is no certain knowledge as to the size of the infectious particles concerned in the origin of human inhalation tuberculosis, there is considerable circumstantial evidence to suggest that the entities involved are much smaller than the limits of ordinary visibility (1). As is well known, primary pulmonary tuberculosis in man takes root not in the upper respiratory passages but deep in the lung parenchyma, usually beneath the pleura. It is reasonable to assume, therefore, that the effective pathogenic units are smaller than the lumina of the terminal bronchioles. That the tubercle-bacilli-containing-particles responsible for the inception of naturally acquired air-borne pulmonary tuberculosis in rabbits are of microscopic dimensions was indicated by the effect of ultraviolet irradiation of the air of a room contaminated by tubercle bacilli derived from tuberculous animals. Such irradiation protected rabbits from an airborne contagion that caused progressive tuberculosis in 73 per cent of animals of the same genetic resistance to tuberculosis exposed to the same contagion for the same period of one year in an unirradiated room (2). As the ventilation of the irradiated room was such that some droplet nuclei of tubercle bacilli floating in the air were exposed for as short a period as only one second to 2537 Å ultraviolet energy of an average maximum intensity of 200 μ W per cm^2 before their inhalation by the exposed rabbits, and as these particles were sterilized, as shown by failure of the animals to develop tuberculosis, it is likely that the infectious units are microscopic.

Therefore, it was not at all certain whether gauze masks with pores of relatively large magnitude, such as may be worn by individuals exposed to airborne contagion of human tuberculosis, would filter out the highly dangerous invisible droplet nuclei of tubercle bacilli. There is some evidence that six layer gauze masks, especially after repeated washing, will remove bacteria floating in the air and yet will not interfere significantly with the free passage of air necessary for respiration (3).

Miss Esta H. McNett, of the Veterans Administration, who devoted many years of effort toward devising means of protecting nurses engaged in the care of tuberculous patients, has designed a six-layered gauze mask to be worn by

[1] From the Henry Phipps Institute of the University of Pennsylvania, Philadelphia, Pennsylvania.

[2] Aided by grants from the Commonwealth Fund, the Ella Sachs Plotz Foundation and the National Tuberculosis Association.

[3] Presented before the Conference on Tuberculous Nursing, as part of the symposium on *Ways to Enhance the Value of Services*, at the 44th annual meeting of the National Tuberculosis Association, New York, New York, June 14, 1948.

[4] Tuberculosis Control Division, Public Health Service, Federal Security Agency.

these nurses. She approached the writers with the problem of determining the efficiency of such masks. It was largely due to her unrelenting efforts that this study was undertaken. Since the writers had constructed an apparatus for quantitative air-borne infection largely modelled after the one described by Wells (4), an opportunity was at hand to determine whether the gauze masks noted above are protective against the quantitative inhalation of droplet nuclei of tubercle bacilli which regularly induce pulmonary tuberculosis in rabbits.

MATERIALS AND METHODS

As the apparatus used in these experiments will be described in detail elsewhere, only the essential features of the instrument need be presented here. A nebulizer generated droplet nuclei of tubercle bacilli. Most of these nuclei contained isolated bacilli; only occasionally were minute clumps, not larger in diameter than a red blood cell, liberated into the air. This infected air was drawn through a long pipe to an exposure chamber; the heads of the rabbits to be exposed protruded into this chamber through an iris diaphragm collar which fitted closely about their necks. The remainder of the body of the rabbit was within a cylinder into which the collars fitted and both were sealed against leakage of air by appropriate rubber gaskets. The infected air circulated past the noses of the rabbits and was removed from the chamber through an exhaust pipe by the draught action of a big flame at the bottom of a specially constructed chimney and, after its incineration by the flame, was drawn to the outdoor atmosphere by a fan. The number of viable bacillary units present in a unit volume of air breathed by the rabbits was culturally determined (5) by a Wells air centrifuge which impinged known volumes of air into a suitable fluid by its high centrifugal action.

Three and six layer gauze masks, 40 by 44 threads to the square inch, were sewn to fit the contour of the rabbit's head, neck and ears by Miss McNett. Each mask slipped over the rabbit's head like a hood and was provided with appropriately shaped pockets into which the ears protruded. The masks were so sewn that the gauze in front of the rabbit's nose and mouth had no seams. The masks extended backward over the rabbit's neck and beyond the iris diaphragm of the collar described above. In this way the fullest possible benefit that could be afforded by the filtering capacity of the masks was utilized. Figures 1 and 2 illustrate the position of the rabbit in the cylinder and the manner of application of the mask.

Rabbits without masks and rabbits wearing masks were exposed simultaneously to the inhalation of air containing droplet nuclei of highly virulent bovine tubercle bacilli of the Ravenel strain. The arrangement of the rabbits in the exposure chamber is illustrated in figure 3.

EXPERIMENTAL

The apparatus afforded portholes for the exposure of 6 rabbits during each experiment. Ten such experiments have been completed. In each experiment

---

PLATE 1

FIG. 1. Rabbit with collar adjusted about its neck is being placed in the cylinder.

FIG. 2. The photograph on the left shows adjustable rubber-reamed iris diaphragm collar. The middle photograph shows how the gauze mask is secured in position by the collar.

FIG. 3. A masked and an unmasked rabbit inside the exposure chamber where they simultaneously inhale air contaminated by droplet nuclei of tubercle bacilli.

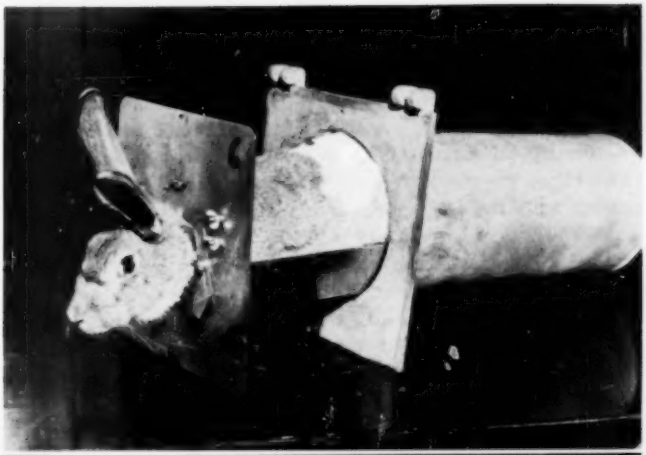

Fig. 1

Fig. 2

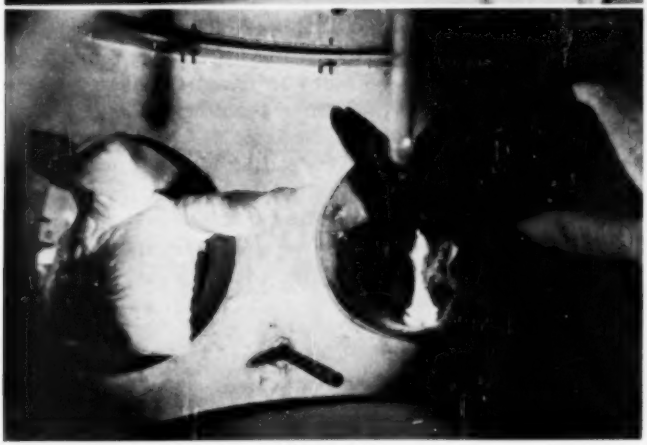

Fig. 3

Plate 1

6 rabbits were exposed simultaneously, 4 without masks and 2 with masks. Two of the 4 rabbits without masks were killed immediately after exposure in order to determine the number of units of living tubercle bacilli retained by the lungs. The lungs were removed under sterile conditions, the bronchi cut at their junction with the lung parenchyma and weighed. The specimens were ground in sterilized, chilled Waring blendors with 9 volumes of cold M/15 Na_2HPo_4 for four minutes. Aliquot portions of this lung tissue brei, as well as portions of the same suspensions treated with 6 per cent sulfuric acid, were planted on a modified Löwenstein's medium (5). The number of colonies derived from a known weight of lung parenchyma indicated the total number of viable bacilli present in both lungs. This procedure makes possible the determination of the minimum number of bacillary units retained by the lung parenchyma.

The remaining 4 rabbits were allowed to live until the control unmasked rabbits developed strong tuberculin reactions. All of the 4 rabbits were then killed and the number of primary tubercles present in their lungs was accurately determined by excising each individual primary focus, except as otherwise indicated.

The results are presented in table 1. In columns 3 and 4 of the table are listed the number of bacillary units isolated from the lungs of rabbits without masks which were killed immediately after exposure. With few exceptions, considerable numbers of tubercle bacilli were isolated in each instance. These ranged from 30 to over 1,000 and averaged 275 tubercle bacilli units per rabbit. Every one of the rabbits that survived four or more weeks, exposed without masks, developed primary tubercles which ranged in number from 3 to 136 and averaged 28 tubercles per animal. Twelve of the 20 masked rabbits which were simultaneously exposed, and killed at the same time as the controls, showed no grossly visible tubercles. Two such examples of the effectiveness of the gauze mask in the protection against tuberculosis are illustrated in figures 4 and 5. The remaining masked rabbits were not completely protected. While the rabbits without masks exposed simultaneously with the masked animals developed from 3 to 136 tubercles and averaged about 31 per rabbit, the masked rabbits developed from 1 to 9 tubercles and averaged less than 4 per rabbit. Thus, even in the instances where the masks failed to afford complete protection, they prevented the inhalation of infectious particles to such an extent that the number of tubercles developed was reduced eightfold.

If the total number of tubercles developed by the 18 rabbits without masks is compared to the total number of tubercles developed by the 19 masked rabbits simultaneously exposed, the resulting values are 28 tubercles per rabbit for unmasked animals and 1.4 tubercles per rabbit for the masked animals. This represents a 95 per cent efficiency for the mask in suppressing grossly visible primary pulmonary tubercles.

In an effort to eliminate the role of variations in individual resistance to tuberculosis, another experiment was done. Six inbred rabbits, of the cross between the A and D families (6), were exposed simultaneously to the inhalation of large

numbers of droplet nuclei of tubercle bacilli of the Ravenel strain. Three were masked and three were without masks. The results are presented in table 2.

TABLE 1

Efficiency of gauze masks in the protection of rabbits against the inhalation of droplet nuclei of tubercle bacilli

EXPERIMENT NUMBER	MASK NUMBER AND TIMES USED PREVIOUS TO EXPERIMENT	CONTROL				MASKED	
		Number of tubercle bacilli cultured from both lungs		Number of tubercles in both lungs		Number of tubercles in both lungs	
		Rabbit 1	Rabbit 2	Rabbit 3	Rabbit 4	Rabbit 5	Rabbit 6
1	No. 1, 0 No. 2, 0	—	29	4	3	1	0*
2	No. 1, 1 No. 2, 1	—	75	3	6	1	0
3	No. 1, 2 No. 2, 2	255	317	59‡	44	0?‡	0
4	No. 2, 3 No. 3, 0	—	—	**	3	0	0
5	No. 2, 4 No. 3, 1	33	29	12‡	4	0?‡	0
6	No. 5, 0 No. 6, 0	720	—	21	23	***	0
7	No. 7, 0 No. 8, 0	146	—	7	****	3	0
8	No. 9, 0 No. 10, 0	54	1,027	27	32	0	3
9	No. 1, 3 No. 2, 5	131	530	60	15	0	1
10	No. 1, 4 No. 2, 6	222	287	54	136	9	9

* Died one day after exposure; no tubercle bacilli could be demonstrated in the lungs by culture or guinea pig inoculation.

** Died one day after exposure; 47 tubercle bacilli cultured from lungs.

*** Died immediately after exposure; tubercle bacilli demonstrated in lungs by guinea pig inoculation.

**** Died four days after exposure; 172 tubercle bacilli cultured from lungs.

‡ Number of tubercles determined by careful inspection and palpation.

The number of bacilli inhaled was such that the unprotected rabbits developed 126, 219, and 223 tubercles, respectively, in the lungs five weeks after exposure. On the other hand, of the masked rabbits, two, which were killed simultaneously

FIG. 4

FIG. 5

FIG. 4. The lungs of rabbit M-13 (unmasked) and of rabbit M-17 (masked), at autopsy thirty-four days after a simultaneous exposure to droplet nuclei of virulent bovine type tubercle bacilli. Fifty-nine primary tubercles were counted in the lungs of the control rabbit (M-13). No tubercles were seen in the masked animal (M-17).

FIG. 5. The lungs of rabbit M-25 (unmasked) and of M-26 (masked) at autopsy forty-four days after a simultaneous exposure to droplet nuclei of virulent bovine type tubercle bacilli. Twelve primary tubercles were counted in the lungs of the control rabbit M-25. No tubercles were seen in the masked animal (M-26).

TABLE 2

Efficiency of gauze masks in the protection of rabbits against the inhalation of droplet nuclei of tubercle bacilli—Experiment II

	CONTROL			MASKED		
RABBIT NUMBER	A D 2-31	A D 3-9	A D 3-5	A D 3-4	A D 2-37	A D 2-28
Mask number and times used previous to experiment	none	none	none	No. 3, 3	No. 2, 7	No. 1, 5
Number of tubercles in both lungs	223	126	219	60	7	0*

* Rabbit died 3 days after exposure; no tubercle bacilli could be obtained from the lungs by culture or guinea pig inoculation.

with the control rabbits, had 60 and 7 tubercles, respectively, in their lungs. One rabbit died three days after exposure. No tubercle bacilli could be demonstrated either by culture or guinea pig inoculation in this rabbit's lung. Thus, the efficiency of the masks in this experiment, based on the standards outlined above, was approximately 88 per cent, which is not materially different from that in the previous 10 experiments.

Addition of the results obtained with these 6 rabbits exposed to massive numbers of tubercle bacilli to those listed in table 1 reveals an average of 51 tubercles per rabbit in the unmasked animals and 4.3 tubercles per rabbit in the masked animals, or a mask efficiency of approximately 92 per cent.

In column 2 of table 1 are given the serial numbers of the masks used for each rabbit. In each experiment the number of the mask listed first was used for rabbit 5 and the mask listed second was used for rabbit 6. In the same column are indicated the number of times each mask was used and the number of times it had been washed and autoclaved before further use. In some experiments the masks consisted of six layers of gauze, in others they were three-layered. It will be noted that no consistent difference in the efficiency of these masks was found under these varying conditions.

DISCUSSION

It has been found in this study that, if all the air respired by rabbits exposed to the inhalation of droplet nuclei of virulent bovine tubercle bacilli passes through three or six layer gauze masks, there is a 90 to 95 per cent reduction in the incidence of primary pulmonary tuberculous foci which develop within five weeks. It would follow, therefore, that, if the respired air contains but a few bacilli, the masked animal will usually be protected from an otherwise fatal infection. Indeed, 12 of 20 masked animals were completely protected against air-borne contagion of such intensity that from 29 to 1,027 tubercle bacilli units were deposited in the lungs of simultaneously exposed unmasked rabbits.

Measurements of the thread diameters and interthread spaces of these masks showed (7) that the superimposition of three to six layers of this material would occlude practically all of the spaces and in this way explain the results of the experiments.

It is not unreasonable to assume that the depth and force of the inspiration of the rabbits during their exposure, which varied with each animal, may be a determining factor. The deeper and more forceful their inspiration, the less effective may be the filtering capacity of the masks. This remains to be determined. There are many other facts which can be ascertained relative to this problem by the methods described in this paper.

In applying these data to the protection of human beings one must be extremely guarded. The masks were so applied to the rabbits that all of the respired air passed through the masks. To be equally effective for human beings exposed to air-borne infection of tuberculosis, the mask must be worn in an equally effective manner. It would seem that this offers no insurmountable difficulty. If the frame into which the mask fitted could be constructed of pliable material

which could be accurately applied to the contour of the individual's face around the nose and mouth, and if this contact could be made airtight, there is no reason to believe that the mask could not effectively filter out the dangerous invisible particles that are concerned with the inception of pulmonary tuberculosis. The masks protected rabbits from air populated with droplet nuclei of tubercle bacilli to a degree that would be rarely, if ever, found in the air respired by human beings. For, as is well known, human primary tuberculosis usually originates as a single pulmonary focus, whereas the unmasked rabbits in these experiments developed an average of 51 primary tubercles. Nevertheless, it seems reasonable to advise persons wearing masks for this purpose to refrain from deep inspiration as much as possible as it is not unlikely that forceful suction produced by deep inhalation may diminish the filtering efficiency of the masks.

Conversely, as has been shown by Jennison (8), masks worn by coughing patients can hardly be expected to retain the invisible droplet nuclei containing tubercle bacilli propelled through them by the often extremely forceful expiratory chest movements during fits of coughing.

SUMMARY

Under the conditions of these experiments, from 90 to 95 per cent of pathogenic droplet nuclei of virulent bovine tubercle in the respired air can be removed by gauze masks properly worn by rabbits during quiet breathing of heavily infected air.

A method is described by which much pertinent information in regard to this problem can be acquired.

The application of these data to the wearing of masks by human beings exposed to air-borne tuberculous contagion is discussed.

SUMARIO

La Eficacia de las Máscaras de Gasa para la Protección de los Conejos contra la Inhalación de Núcleos de Bacilos Tuberculosos en Gotillas

En las condiciones de los experimentos descritos, pueden eliminarse del aire respirado de 90 a 95 por ciento de los núcleos en gotillas patógenas de bacilos bovinos virulentos, por medio de máscaras de gasa debidamente puestas en conejos, durante la respiración tranquila de aire intensamente infectado.

Descríbese un método que permite adquirir mucha información pertinente acerca de este problema.

Se discute la aplicación de los datos obtenidos al uso de máscaras por los seres humanos expuestos al contagio tuberculoso por vía aérea.

Acknowledgment

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PULMONARY RESECTION IN THE TREATMENT OF TUBERCULOSIS[1, 2]

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INTRODUCTION

Surgical collapse therapy in the treatment of pulmonary tuberculosis has progressed to the stage where indications for operative interference have been well established and final results can be predicted with more than a reasonable degree of assurance. There remains, however, a certain group of patients who have failed to convert after the use of conventional methods of surgical collapse and who need further surgical measures to rid them of active tuberculous foci. Therefore, it is not surprising that pulmonary resection, so successful in its application in the treatment of various nontuberculous lesions, should have been tried in these cases.

In 1942 Thornton and Adams (1) collected and reported the cases of resection for pulmonary tuberculosis. There were 29 cases of pneumonectomy with a mortality of 45 per cent and 46 cases of lobectomy with a mortality of 25 per cent. The group varied so greatly that it was impossible to evaluate the results.

Recently Janes (3), Maier and Klopstock (5), Overholt *et al.* (7), Sweet (21), Bailey (9), and Clagett and Seybold (14) have reported larger individually controlled groups. The results of these studies show a more encouraging picture as to early operative mortality and end results. The improvement in the results is to be expected in view of the refinements in surgical technique employed in dealing with the hilar structures. More recently, however, Alexander (10) has compiled the largest group of cases (411) and found that only 45 per cent are apparently well and without tubercle bacilli in their sputum, 25.5 per cent are dead, and 29.5 per cent of the whole group have active uncontrolled disease. A study of such a large group demonstrates quite clearly that resection, as used to date, is not the answer to the problem.

The present report deals with 80 resections performed at the State of Wisconsin General Hospital over a period of three years. The patients were referred from various sanatoriums throughout Wisconsin. Most of them had had some type of collapse therapy prior to admission and they represented a group in need of further treatment. After thorough study they were brought before the combined medical and surgical staffs concerned with the treatment of pulmonary tuberculosis. Further measures were discussed and decided upon. In this group of patients such a concerted study was preferred to the decisions of only one or two individuals.

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[2] Presented before the Medical Section, as part of the *Symposium on Surgery—Trends—Late Results*, at the 44th Annual Meeting of the National Tuberculosis Association, New York, New York, June 16, 1948.

OPERATION

The operative technique employed was quite similar to that used by others. The patient was placed on his less involved side. If there was excessive bronchial secretion, a bronchoscopy was done and the offending side plugged with a Tampax pack. The anesthetic agent varied and consisted for the majority of the patients of cyclopropane induction followed by ether. The incision most recently employed was that used for first-stage thoracoplasty. This is of definite advantage if thoracoplasty is to be performed at the same sitting. The sixth or seventh rib was resected after the intercostal nerves of the resected and adjoining ribs were crushed to reduce postoperative pain. Following resection, one gram of streptomycin and 100,000 units of penicillin were introduced into the pleural space. No drainage was used following pneumonectomy but in all cases of lobectomy drainage was instituted and maintained for at least forty-eight hours. If additional air or fluid accumulated after removal of the tube, aspiration was done promptly to promote complete expansion of the remaining lobe or lobes. The intrapleural pressure was kept negative following pneumonectomy. Thoracentesis was repeated every other day. Fluid was withdrawn, one-half gram of streptomycin instilled, and the pleural pressure readjusted. These procedures were continued until the pleural space was obliterated and fluid no longer accumulated. Patients who had had a previous thoracoplasty were observed closely because the small pleural space following pneumonectomy reacted quickly, and at times violently, to minor pressure changes. It is felt that the early obliteration of the pleural space has been most valuable in preventing the development of early and late tuberculous empyema. Upper stage thoracoplasty was done at the time of resection if the condition of the patient permitted. If not advisable then, it was carried out as soon afterwards as possible.

Phrenicectomy was done routinely following pneumonectomy but the function of the diaphragm was preserved following lobectomy to ensure normal activity of the remaining lobe and as a guard against atelectasis. Bronchoscopy was used immediately postoperatively only if secretions had been troublesome during the operation. Blood transfusions were used freely during the operation and throughout the postoperative period. The patient was placed in the Trendelenberg position for the first twenty-four hours. Frequent vigorous changes in position were mandatory. Subcutaneous and intravenous fluids were given until the patient was able to maintain his fluid balance. The patient was returned to the sanatorium as soon as he was judged fit to travel by ambulance.

INDICATIONS

Many factors enter into the consideration of any patient as a candidate for resection. Nevertheless, certain broad indications must be adopted in order to have a starting point. The indications used in this group of patients conform surprisingly well to those followed by a number of other surgeons (table 1).

Thoracoplasty failure: The group of patients in whom thorocoplasty had failed represented the chief indication for resection (tables 2 and 3). There were 41 such cases (51.25 per cent). Twenty-six (32.5 per cent) had pneumonectomy and fifteen (18.75 per cent) had lobectomy. Frequently there were other important lesions present, some of which may be considered as definite indications for resection; but these were considered secondary if a previous thoracoplasty had been performed. Seventeen patients had received pneumothorax, 12 had stenosis of the lobar or stem bronchus, 7 showed severe bronchiectasis, 6 had repeated

pulmonary hemorrhages, and 2 had empyema, one tuberculous, the other a mixed infection. The lobectomy group contained 9 with bronchiectasis, 8 with cavity or cavities, 3 with atelectasis, 2 with recurrent hemoptysis, and one with lobar stenosis.

TABLE 1

Broad indications for resection (various surgeons)

NAME	THORACOPLASTY FAILURE	BRONCHOSTENOSIS	TUBERCULOMA	LOWER LOBE AND BASAL CAVITIES	TUBERCULOUS BRONCHIECTASIS	GIANT CAVITY DESTROYED LUNG	PNEUMOTHORAX FAILURE
Adams (2)	+		+	+	+	+	
Alexander (11)	Patients for whom collapse therapy is unsuitable or for whom it has been tried unsuccessfully						
Clagett (13)	+	+	+		+	+	
Dolley (12)	+	+		+	+	Tension cavity	
Janes (4)	+	+	+	If pneumothorax or phrenic surgery fails			+
Jones (15)	+	+	+	+	+		+
Kinsella (16)	+	+			+		
Maier (6)	+	+	+	+	+	+	+
O'Brien (17)	+	Over 70 per cent	+	+	Does not respond to streptomycin or is very extensive.		+
Ochsner (18)	+	+	+				
Overholt (8)	+	+	Of size	+	+	+	
Samson (19)	+	+	+	+	+	+	
Strieder (20)	+	+	+		+	Tension cavity	
Sweet (22)	+	+	+	+	Distal to obstruction.		
Woodruff (23)	+	High grade	+	+			
Authors	+	+	+	+	+	+	+

Bronchostenosis: The second most common indication for resection was bronchostenosis, which was present in 16 cases (20 per cent). Thirteen (16.25 per cent) of this group had pneumonectomy and 3 (3.75 per cent) lobectomy (tables 4 and 5). In the pneumonectomy group there were 5 cases of atelectasis,

TABLE 2

Thoracoplasty failure (lobectomy)

PATIENT, AGE, SEX	STAGE DURATION PREVIOUS THERAPY	INVOLVEMENT	LOBECTOMY DATE	POSTOPERATIVE COURSE	PRESENT STATUS
F. N. 52 M	II, 5 years Thoracoplasty	Bronchiectasis RU and ML, pneumonitis	RU and ML 4-24-45	Continued improvement	9-1-47 "negative" sputum, full time work
C. P. 33 F	III, 3 years Phrenic surgery, thoracoplasty, revision	Cavity RUL, bronchiectasis, atelectasis, bronchitis	RUL 5-23-45	Uneventful	January 1948 "negative" sputum, working as nurse, symptom free
E. P. 27 F	III, 3 years Pneumothorax, pneumoperitoneum, thoracoplasty	Cavity LUL	LUL 5-24-45	Died in October 1947. Spread to contralateral lung	Dead
K. R. 24 M	III, 5 years Pneumothorax, thoracoplasty	Bronchiectasis LUL with hemoptysis	LUL 10-1-46	Severe dyspnea for 4 weeks because of low respiratory reserve	9-5-47 "negative" sputum, at home, working, roentgenograms stable
A. B. 36 F	III, 8 years Phrenic surgery, thoracoplasty, revision	Bronchiectasis and cavity RUL, stenosis UL bronchus	RU and ML 11-30-46	Atelectasis RLL for 4 days	9-1-47 "negative" sputum, at home, continued well
L. B. 23 M	III, 6 years Thoracoplasty	Atelectasis RUL with bronchiectasis	RU and ML 2-24-47	Vertigo due to streptomycin	9-24-47 "negative" sputum, 12-20-47 "negative" sputum, rehabilitation at sanatorium
A. W. 45 M	III, 4 years Pneumothorax, thoracoplasty	RU and ML Bronchiectasis	RU and ML 2-26-47	Uneventful	9-1-47 "negative" sputum, no change January 1948, 4-15-48 "negative" sputum
V. O. 26 M	II, 5 years Phrenic surgery, thoracoplasty	Bronchiectasis RUL	RUL 3-27-47	Developed cavity in contralateral upper lobe November 1947 closed and remained closed	9-1-47 "negative" sputum, 1-19-48 "negative" sputum
A. W. 33 M	III, 9 years Thoracoplasty, revision, pneumothorax on opposite side	Cavity RUL	RU and ML 7-18-47	Dyspnea and palpitation, responded slowly	8-14-47 sputum positive for tubercle bacilli, 4-15-48 sputum positive for tubercle bacilli
R. B. 44 M	III, 3 years Thoracoplasty for tension cavity	Large cavity RUL, hemoptysis, red bronchus	Ru and ML 9-17-47	Slow continued improvement	10-29-47 sputum positive for tubercle bacilli, 3-1-48 "negative" sputum following three cultures

TABLE 2—*Concluded*

PATIENT, AGE, SEX	STAGE DURATION PREVIOUS THERAPY	INVOLVEMENT	LOBECTOMY DATE	POSTOPERATIVE COURSE	PRESENT STATUS
H. D. 27 F	III, 5 years Thoracoplasty	Multiple cavities RUL, bronchiectasis	RUL 10-15-47	Atelectasis of M and L immediately postoperatively subsided	3-9-48 "negative" sputum, roentgenograms stable
M. A. 38 F	III, 12 years Thoracoplasty	Cavity RUL	RUL 10-24-47	Reactivation of tuberculosis otitis media	11-8-47 "negative" sputum, 4-1-48 "positive" sputum, otherwise excellent
H. S. 52 M	III, 3 years Thoracoplasty	Cavity and bronchiectasis RUL	RUL 10-24-47	Chest has remained stable	11-18-47 "negative" sputum, 4-15-48 "negative" sputum
I. M. O. 36 F	III, 9 years Pneumothorax, thoracoplasty	Atelectasis and fibrosis LUL	LUL 12-22-47	Auditory and visual hallucinations	4-15-48 "negative" sputum
E. L. 43 F	III, 15 years Thoracoplasty	Large thin-walled at medial side of left apex	LUL 2-10-48	Uneventful	4-15-48 sputum "negative" on smear

2 with repeated hemoptysis, and 3 with cavities. One patient (M.M.) did not have a thoracoplasty following lobectomy and developed a "spread" in the apex of the right lower lobe eight months later. A thoracoplasty was performed to control the "spread."

Tuberculous bronchiectasis: The third most common indication, tuberculous bronchiectasis, concerned only 8 cases (10 per cent). All patients in this group had lobectomy with the removal of one or two lobes. Two had cavitation of the involved lobe, in addition one had repeated hemoptyses, and one a contralateral pneumothorax at the time of resection. Three patients had thoracoplasty performed at the time of lobectomy, and three soon thereafter. One patient (M.M.) had a segmental resection of the apex of the lower lobe. This was the only time segmental resection was done in the entire series. One postoperative death occurred.

Lower lobe lesions: The group of lower lobe lesions consisted of 4 cases (table 7). The patient (J.DeS.) might have been placed in another group but the existence of a tuberculoma in the lower lobe would appear to justify his being included here.

Pneumothorax failure: Four cases with unsuccessful pneumothoraces have been included (table 8). One patient (C.S.) suffered a spontaneous collapse as the first recognized symptom early in the course of his disease; this resulted in a tuberculous empyema and a nonexpansile lung. Two patients had nonexpansile lungs. One patient had a thick-walled cavity in a well collapsed right upper lobe. Two had lobectomy, one with decortication and expansion of the remaining lobe, while 2 had pneumonectomy. All received a later thoracoplasty.

Destroyed lung: Three patients had far advanced lesions with widespread

TABLE 3

Thoracoplasty failure (pneumonectomy)

PATIENT, AGE, SEX	STAGE DURATION PREVIOUS THERAPY	INVOLVEMENT	PNEUMONECTOMY DATE	POSTOPERATIVE COURSE	PRESENT STATUS
H. S. 36 F	III, 8 years Sanatorium, phrenic surgery, pneumothorax, thoracoplasty	Stenosis LUL bronchus, atelectasis of UL	Left 12-7-44	Coughed up silk sutures 6 months later; spread to right lung which cleared; reactivation right lung February 1948	11-25-47 sputum "positive," 4-15-48 sputum "positive"
I. M. 38 F	III, 5 years Sanatorium, phrenic surgery, thoracoplasty	Extensive cavitation, (Destroyed lung)	Right 5-21-45	Uneventful	3-1-47 sputum "negative," continued well, 4-15-48 full time work
L. W. 33 M	III, 5 years Pneumothorax, thoracoplasty, revision	Persistent cavity, hemoptysis	Right 6-20-45	Hemothorax, postoperatively controlled	9-1-47 sputum "negatives," TB sinus chest wall, Reoperated 4-15-48 negative)
S. L. 38 F	III, 15 years Phrenic surgery, thoracoplasty, revision	Bronchiectasis, high grade stenosis right stem bronchus	Right 10-26-45	Uneventful	4-15-48 sputum "negative," part time work, low pulmonary reserve as before operation
T. E. 46 M	III, 4 years Pneumothorax, thoracoplasty	Stenosis RUL bronchus, mixed infection empyema	Right 4-30-46	Immediate reactivation on left with effusion, cleared with streptomycin	3-9-48 sputum "negative"
A. K. 40 F	II, 10 years Phrenic surgery, pneumothorax, thoracoplasty	RUL cavitation, bronchiectasis, red bronchus	Right 6-14-46	Uneventful	9-1-47 sputum "negative," at home; January 1948 continues well; excellent
E. L. 25 F	III, 7 years Pneumothorax, phrenic surgery, thoracoplasty	Atelectasis with tuberculous bronchitis	Right 6-20-46	Uneventful	9-1-47 sputum "negative," full time work, continues well 4-15-48
V. K. 20 F	III, 6 years Pneumothorax, thoracoplasty	RUL bronchial stenosis, atelectasis of right lung with cavity	Right 7-2-46	Ulceration of bronchial stump, visible silk sutures, to be removed	12-1-47 sputum "positive," should clear with removal of silk sutures
L. K. 29 M	III, 4 years Pneumothorax, thoracoplasty	Stenosis of left stem bronchus; tuberculous bronchitis, active	Left 7-3-46	Reactivation on right August 1947 after discharge from sanatorium, cleared with streptomycin	10-2-47 sputum "positive," 4-15-48 sputum "negative"
A. B. 38 M	III, 13 years Phrenic surgery, pneumothorax, thoracoplasty	Cavitation LUL, stenosis stem bronchus, suppurative pneumonitis	Left 2-10-47	Continued improvement	9-1-47 sputum "positive," 1-24-48 sputum "negative," 2-28-48 sputum "negative," at home
E. F. 54 M	III, 9 years Thoracoplasty	Persistent cavitation, intermittent hemoptysis	Right 3-11-47	Died suddenly 9-7-47 of coronary occlusion	Sputum "negative" 9-1-47 six days before death

TABLE 3—*Continued*

PATIENT, AGE, SEX	STAGE DURATION PREVIOUS THERAPY	INVOLVEMENT	PNEUMONECTOMY DATE	POSTOPERATIVE COURSE	PRESENT STATUS
F. S. 27 F	III, 2 years Thoracoplasty	Fibrocaseous tuberculosis with cavitation, bronchiectasis and increasing atelectasis	Right 3-11-47	Reactivation at left apex, streptomycin for 90 days halted disease, now stable	9-1-47 sputum "positive," 2-28-48 sputum "negative"
C. R. 22 F	III, 6 years Pneumothorax, thoracoplasty	Fibrocaseous with cavitation, stenosis right stem bronchus	Right 3-25-47	Ulceration of bronchial stump 10-1-47, cleared following streptomycin for 150 days	9-1-47 sputum "positive," 2-15-48 sputum "negative"
S. M. P. 44 F	III, 19 years Thoracoplasty	Pyogenic infection superimposed on cavernous lesion, uncontrolled cough	Left 5-2-47	Streptomycin reaction, cyanosis, dyspnea; a respiratory cripple	9-1-47 sputum "positive," dyspnea improving, died 2-28-48 cardiac failure
M. K. 41 F	III, 6 years Phrenic surgery, pneumothorax, pneumoperitoneum, thoracoplasty	Bronchiectasis RU and ML, repeated hemoptysis	Right 5-10-47	Complicating peptic ulcer, bleeding; lung stable	10-1-47 sputum "negative;" continues well 4-15-48
N. D. P. 44 M	III, 7 years Pneumothorax, pneumoperitoneum, phrenic surgery, thoracoplasty	Extensive lesions throughout lung, active bronchitis cleared with streptomycin	Left 7-28-47	Convalescence satisfactory, now in rehabilitation in sanatorium	1-5-48 sputum "negative"
A. J. 34 F	III, 8 years Thoracoplasty, revision	Stenosis RUL bronchus, cavitation U and LL, bronchiectasis	Right 9-11-47	Left lung has remained stable	4-15-48 sputum "negative"
I. W. 44 F	III, 5 years Permanent, phrenic surgery, thoracoplasty	Pinpoint stenosis, suppurative pneumonitis, hemoptysis, bronchiectasis	Left 9-15-47	Right lung continued to remain quiescent	1-4-48 sputum "negative," on rehabilitation in sanatorium
E. T. 28 F	II, 7 years Phrenic surgery, thoracoplasty	Fibrocaseous tuberculosis, bronchiectasis, repeated hemoptysis	Left 10-10-47	Rapid convalescence	12-20-47 sputum "negative," right lung normal 3-24-48
F. R. 21 M	III, 2 years Phrenic surgery, pneumoperitoneum, thoracoplasty	Multiple bronchiectatic cavitation, repeated hemoptysis	Left 10-16-47	Has remained quiescent since operation	Six sputum "negative" cultures since operation
M. G. 28 F	III, 8 years Phrenic surgery, thoracoplasty	Stenosis left stem bronchus, many bronchiectatic cavities, cavities in LL	Left 11-28-47	Streptomycin started 3-4-48, no evidence of spread or reactivation	3-24-48 sputum "positive"
L. Y. 21 F	III, 4 years Thoracoplasty	Multiple cavities, bronchiectasis	Left 12-3-47	Right lung has continued to remain stable	1-2-48 sputum "negative"

TABLE 3—*Concluded*

PATIENT, AGE, SEX	STAGE DURATION PREVIOUS THERAPY	INVOLVEMENT	PNEUMONECTOMY DATE	POSTOPERATIVE COURSE	PRESENT STATUS
C. L. 48 M	III, 9 years Pneumothorax, oleothorax, thoracoplasty, streptomycin	Pinpoint stenosis stem bronchus, cavity at apex, tuberculous empyema	Left 12-8-47	Condition has gradually improved	2-8-48 sputum "negative"
M. M. 22 F	III, 3 years Pneumothorax, promine, thoracoplasty	Bronchiectasis, stricture LL bronchus, atelectasis	Left 12-18-47	Patent ductus ligated at operation	1-4-48 sputum "negative," right lung stable
M. H. 26 F	III, 5 years Thoracoplasty, 1945	Swelling of right stem bronchus, bronchial "spread"	Right 2-4-48	Continued improvement	4-15-48 sputum "negative"
D. W. 30 F	III, 5 years Phrenic surgery, right 1944; thoracoplasty, right 1946	Tuberculous granulations in right stem bronchus, mucopurulent secretions	Right 2-12-48	Continued improvement	4-15-48 sputum "negative"

TABLE 4

Bronchial stenosis (lobectomy)

PATIENT, AGE, SEX	STAGE DURATION PREVIOUS THERAPY	INVOLVEMENT	LOBECTOMY DATE	POSTOPERATIVE COURSE	PRESENT STATUS
M. M. 31 F	II, 3 years Pneumothorax, pneumonolysis, phrenic surgery	Stenosis of RUL bronchus with atelectasis; recurrent pneumonitis	RUL 9-14-46	Thoracoplasty in May 1947 for basal spread	February 1948 gastric culture "negative"; starting exercise in sanatorium; condition excellent
V. T. 27 M	III, 3 years Pneumothorax, pneumonolysis, phrenic surgery	Bronchitis right stem bronchus; recurrent pneumonitis, cavities in LL	RM and LL phrenic 8-15-46	Continued improvement	9-7-47 "negative" sputum, slight dyspnea on extreme exertion; "negative" sputum, February, 1948
L. M. 26 F	II, 5 years Phrenic surgery, extrapleural pneumothorax	Stenosis RUL bronchus, atelectasis UL; ulcerative bronchitis responded to streptomycin	RUL 10-7-47 Thoracoplasty 10-30-47	Tuberculous laryngitis; streptomycin 12-29-47 to 3-2-48 with great improvement	4-15-48 Repeated sputum cultures "negative"

destruction of lung parenchyma. One patient (B.P.) had a large mixed abscess. These 3 had pneumonectomy followed by thoracoplasty.

Tension cavity and mistaken diagnosis: Only one patient had a true tension cavity (table 10). An upper lobe lobectomy was done without subsequent thoracoplasty in this patient who refused to consider any type of surgery with resultant chest deformity. There were three instances (3.75 per cent) in which

TABLE 5

Bronchial stenosis (pneumonectomy)

PATIENT, AGE, SEX	STAGE DURATION PREVIOUS THERAPY	INVOLVEMENT	PNEUMONECTOMY DATE	POSTOPERATIVE COURSE	PRESENT STATUS
P. S. 18 F	III, 4 years. Sanatorium 4 years, phrenic surgery	Fibroid lesion, atelectasis, pinpoint stenosis left stem bronchus	Left 3-13-46	Rapid convalescence	December 1947 "negative" sputum, at home, attending school
R. B. 22 F	III, 2 years. Pneumothorax	Inexpansile atelectatic lung, high grade stenosis left stem bronchus	Left 12-26-46 Thoracoplasty 1-20-47	Uneventful	9-1-47 "negative" sputum, in sanatorium, 4-20-48 at home
R. S. 29 F	III, 7 years. Pneumothorax, phrenic surgery	Bronchial stenosis, repeated hemoptysis caseous lesions throughout	Left 3-17-47 Thoracoplasty 4-9-47	Chest films continue to remain unchanged	3-4-48 "negative" sputum, at home
R. L. 19 F	III, 4 years. Streptomycin for 4 months in sanatorium	Stenosis of left stem bronchus	Left 3-18-47 Thoracoplasty 4-2-47	Excellent convalescence	3-9-48 "negative" sputum, at home
D. K. 18 F	III, 4 years. Pneumothorax, pneumonolysis, phrenic surgery	Cavitation LUL, stenosis of stem bronchus, recurrent pneumonitis	Left 3-31-47 Thoracoplasty 4-19-47	Continued improvement	4-15-48 "negative" sputum
G. H. 44 M	II, 12 years. Pneumothorax	Stenosis of stem bronchus with widely disseminated disease, cavity UL	Left 5-15-47 Thoracoplasty 6-10-47	Streptomycin 7-24-47 to 9-7-47 because of questionable pericarditis; opposite lung stable	3-15-48 "negative" sputum
A. K. 23 F	III, 6 years. Pneumothorax, phrenic surgery; streptomycin for 90 days in sanatorium 1947	High grade stenosis stem bronchus, scattered tubercles in UL	Left 5-28-47 Thoracoplasty 6-18-47	Satisfactory convalescence	2-11-48 "negative" sputum, in sanatorium, 4-15-48 at home
J. R. 33 F	III, 6 years. Pneumoperitoneum streptomycin, pneumothorax, 2 phrenic operations	Stenosis of stem bronchus	Right 7-29-47 Thoracoplasty 8-20-47	General condition continues to improve	2-1-48 "negative" sputum
K. P. 28 M	III, 14 years. Sanatorium	Stenosis of stem bronchus with complete atelectasis	Left 8-1-47 Thoracoplasty 8-28-47	Continued improvement in sanatorium	2-1-48 "negative" sputum
A. K. 47 M	II, 1 year Streptomycin 4 months in sanatorium, pneumothorax	Atelectatic left lung with cavity, high grade stenosis	Left 9-29-47	Died of cerebral thrombosis 10-1-47	Dead
W. O. 30 M	III, 5 years. Pneumothorax, pneumonolysis, 2 phrenic operations	Stenosis of RLL bronchus, hemoptysis, bronchiectasis, severe cough	Right 11-10-47 Thoracoplasty 12-3-47	Severe dyspnea for 1 month	Left lung remains stable, 4-15-48 "negative" sputum

TABLE 5—*Concluded*

PATIENT, AGE, SEX	STAGE DURATION PREVIOUS THERAPY	INVOLVEMENT	PNEUMONECTOMY DATE	POSTOPERATIVE COURSE	PRESENT STATUS
A. H. 29 F	III, 18 years Pneumothorax, thoracotomy for mixed infection empyema	Atelectatic lung, complete bronchial stenosis, numerous cavities, bronchiectasis	Left 12-10-47 Thoracoplasty 12-30-47	Streptomycin started 2-21-48 because of reopening of old chest sinus	4-15-48 sputum cultures "negative"
B. B. 21 F	III, 2 years. Pneumoperitoneum, phrenic surgery	50 per cent stenosis of stem bronchus, active bronchitis with no ulceration	Left, with thoracoplasty 1-13-48	Opposite lung has remained stable	4-15-48 "negative" sputum

TABLE 6

Tuberculous bronchiectasis (lobectomy)

PATIENT, AGE, SEX	STAGE DURATION PREVIOUS THERAPY	INVOLVEMENT	OPERATION DATE	POSTOPERATIVE COURSE	PRESENT STATUS
H. M. 28 M	II, 7 years. Pneumothorax, phrenic surgery	Bronchiectasis, repented hemoptysis, cavity LUL	LU lobectomy 2-19-45	Working full time at present, lesion stable by roentgenography	8-1-47 "negative" sputum, full time work, 4-15-48 "negative" sputum
B. H. 59 M	III, 3 years. Bed-rest	Bronchiectasis RU and ML, severe	RU and ML lobectomy 2-16-46	Developed bronchial fistula, putrid empyema	Died 55th postoperative day
B. K. 26 F	II, 6 months. Phrenic surgery, streptomycin 35 days in sanatorium	Bronchiectasis RU and ML, caseous lesions bronchial distribution	RU and ML lobectomy and thoracoplasty 11-12-47	Streptomycin continued until 1-18-48, total of 90 days, chest roentgenogram reveals stable lesions	February 1948 "negative" sputum
P. O. 28 F	II, 2 years Pneumothorax, phrenic surgery	Bronchiectasis, atelectasis RUL	RU lobectomy Thoracoplasty 4-23-47	Roentgenogram reveals stable lesions, streptomycin 8-23-47 to 11-25-47, no source evident	9-1-47 "positive" sputum, 1-29-48 "positive" sputum
M. M. 20 F	III, 4 years. Pneumothorax, phrenic surgery	Bronchiectasis RUL, copious sputum, contralateral pneumothorax	RU lobectomy 8-21-47. Segmental of apex LL. Thoracoplasty 9-13-47	Small bronchopleural fistula with mixed infection, closed with thoracoplasty	10-21-47 "negative" sputum, January 1948 "negative" sputum; condition excellent
M. R. 26 F	II, 9 years. Pneumothorax	Bronchiectasis LUL	LU lobectomy 8-25-47 Phrenic surgery 8-30-47 Thoracoplasty 9-11-47	Continued good during postoperative period	10-21-47 "negative" sputum, January 1948 "negative" sputum; chest stable
S. B. 20 M	III, 2 years. 2 phrenic operations	Bronchiectasis with cavity RUL	RU lobectomy 9-10-47 Thoracoplasty 10-3-47	Temporary atelectasis LL	10-1-47 "negative" sputum, 12-1-47 "negative" sputum; being rehabilitated
H. G. 36 F	III, 1 year. Streptomycin 92 days	Saccular bronchiectasis RUL with cavity	RU lobectomy and thoracoplasty 2-13-48	Uneventful	4-20-48 "negative" sputum

TABLE 7

Lower lobe lesions

PATIENT AGE, SEX	STAGE DURATION PREVIOUS THERAPY	INVOLVEMENT	OPERATION DATE	POSTOPERATIVE COURSE	PRESENT STATUS
M. S. 20 F	III, 2 years. Phrenic surgery	Cavitation RLL, copious sputum, atelectasis RM and LL	RM and LL lobectomy with phrenic surgery 11-7-46	Continued improvement	9-1-47 "negative" sputum; at home; 2-6-48 "negative" sputum; lesion stable by roentgenography.
J. DeS. 22 M	II, 5 years. Rest, pneumothorax unsatisfactory because of adhesions	Tuberculoma LLL, bronchiectasis UL	Pneumonectomy, Lt 4-23-47 Thoracoplasty 6-19-47	Continued improvement since September 1947	9-1-47 "positive" sputum in sanatorium; six "negative" cultures since November, 1947
K. K. 25 M	III, 4 years. Pneumothorax, streptomycin 81 days	Multiple cavities RLL	RLL lobectomy with phrenic surgery 9-20-47	Uneventful, continued improvement in general condition	10-4-47 "negative" sputum; 12-29-47 "negative" sputum
D. F. 17 M	III, 5 months. Rest, streptomycin 45 days	RM and LL atelectasis and cavitation	RM and LL lobectomy with phrenic surgery 11-20-47	Uneventful	2-26-48 "negative" sputum; condition excellent

TABLE 8

Pneumothorax failure

PATIENT, AGE, SEX	STAGE DURATION PREVIOUS THERAPY	INVOLVEMENT	OPERATION DATE	POSTOPERATIVE COURSE	PRESENT STATUS
M. G. 28 M	III, 6 years. Pneumothorax	Nonexpansile left lung with cavity UL	Pneumonectomy, left 8-8-47 Thoracoplasty 8-29-47	Contralateral pleural fluid became purulent with bronchopleural fistula 2-21-48	2-1-48 "positive" sputum; not good
R. M. 42 M	II, 5 years. Pneumothorax, phrenic surgery	RUL cavity failed to close with pneumothorax	RU lobectomy 9-6-47; Thoracoplasty 9-25-47	Wound infection with osteomyelitis of ribs following thoracoplasty, reoperation necessary	4-15-48 "negative" sputum
R. N. 32 M	III, 2 years. Pneumothorax pneumonolysis	Nonexpansile left lung with tuberculous empyema	LU lobectomy with decortication of LL 11-3-47; Thoracoplasty 11-17-47	Uneventful	4-15-48 "negative" sputum
C. S. 33 M	III, 1 year. Sanatorium	Spontaneous pneumothorax, inexpansile lung, tuberculous empyema	Pneumonectomy, left 1-14-48 Thoracoplasty 2-9-48 2-25-48	Uneventful	4-15-48 smears of sputum "negative"

the diagnosis of tuberculosis was overlooked previous to operation. In two older individuals the preoperative diagnosis was bronchogenic neoplasm and in one

TABLE 9

Destroyed lung (pneumonectomy)

PATIENT, AGE, SEX	STAGE DURATION PREVIOUS THERAPY	INVOLVEMENT	PNEUMONECTOMY DATE	POSTOPERATIVE COURSE	PRESENT STATUS
B. P. 30 F	III, 6 years Unsuccessful pneumothorax	Multiple cavities throughout left lung, extensive fibrosis	Left 4-25-47 Thoracoplasty 5-22-47	Atelectasis RUL, cleared	9-1-47 "negative" sputum; gained 20 lbs; 4-3-48 clinically well, at home
F. DeS. 21 F	III, 4 years Phrenic surgery, repeated 1 year later	Cavity RUL, multiple bronchiectatic cavities in lower lobes, ulcerative bronchitis right 10-20-47, red bronchus following streptomycin 11-17-47	Right 11-26-47 Thoracoplasty 12-16-47	Streptomycin started 3-28-48 in sanatorium	4-15-48 "positive" sputum; bronchial ulceration
V. J. 22 F	III, 1 year Pneumothorax, streptomycin 3 months	Atelectatic lung with scattered cavities, infection of left stem bronchus	Left 12-29-47 Thoracoplasty 1-27-48	Continues to improve	4-15-48 "negative" sputum

TABLE 10

Tension cavity (mistaken diagnosis)

PATIENT, AGE, SEX	STAGE DURATION PREVIOUS THERAPY	INVOLVEMENT	OPERATION DATE	POSTOPERATIVE COURSE	PRESENT STATUS
R. G. 28 M	III, 2 years Bed-rest	Tension cavity LUL, refused thoracoplasty	LU Lobectomy 4-10-47	Continued improvement	January 1948 "negative" sputum, playing professional baseball
J. B. 65 M	1 year No treatment	Hilar mass on right, 8 by 8 cm.; bronchoscopy negative	Pneumonectomy, right 10-1-47	Mistaken diagnosis, thought to be cancer, proved to be caseous tuberculosis	Excellent; full time work
L. E. 27 F	III, 1 month	Bronchiectasis, atelectasis of RUL, stenosis of UL bronchus	RU Lobectomy and thoracoplasty 10-11-47	Thought to be a nontuberculous bronchiectasis; sputum "negative" before operation; histopathologic examination revealed tuberculosis	4-15-48 "negative" sputum; excellent
D. H. 59 F	4 to 5 years Deaf mute	Obstruction in LLL bronchus	Pneumonectomy, left 11-18-47 Followed by auricular fibril., cardiac decomp.; digitalis	Thought to be a bronchiogenic cancer before operation	4-15-48 "negative" sputum

other the preoperative diagnosis was nontuberculous bronchiectasis secondary to pneumonia. In all of these patients the roentgenographic appearance was not characteristic of tuberculosis. In addition to these findings, several sputum

smears and cultures examined preoperatively were negative for tubercle bacilli. However, the pathologic picture of the resected tissue was characteristic of tuberculosis.

In table 11 may be seen the number of patients having pneumonectomy and lobectomy under the different indications chosen for resection. The greatest number (41) were performed for thoracoplasty failure. This is not surprising as most of the resections fell under this indication. Forty-seven (58.75 per cent) of the patients had pneumonectomy and 33 (41.25 per cent) had lobectomy.

TABLE 11

Type of operation

INDICATIONS	PNEUMONECTOMY	LOBECTOMY	OPERATIVE DEATHS
Thoracoplasty failure	26	15	—
Bronchial stenosis	13	3	1 (Pneumonectomy)
Tuberculous bronchiectasis	—	8	1 (Lobectomy)
Lower lobe lesions	1	3	—
Pneumothorax failure	2	2	—
Destroyed lung	3	—	—
Mistaken diagnosis	2	1	—
Tension cavity	—	1	—
Total 80 patients	47 (58.75 per cent)	33 (41.25 per cent)	Operative mortality 2.5 per cent

RESULTS

In the entire group of 80 resections there were 2 operative deaths, giving a total series mortality of 2.5 per cent. One patient (B. H.) died on the fifty-fifth postoperative day with a bronchopleural fistula and a mixed empyema. The other (A. K.) died on the first postoperative day. Postmortem revealed the cause of death to be thrombosis of a cerebral artery.

The various postoperative complications are listed in table 12. Some were of a temporary nature but are included to make the report complete and self-explanatory.

The results in relation to indications are presented in table 13. In view of the short period of observation which has passed since many of the resections, it is not surprising that the 52.5 per cent of the total group, who are apparently noninfectious, still remain in the sanatorium. Only 25 patients have been discharged. The total of 83.75 per cent of the series with cultures negative for tubercle bacilli exceeded expectations. A high percentage of reversal of infectiousness occurred in the cases from the three groups representing the most common indications for the procedure.

In table 14 may be seen the final results obtained in the series of 80 patients, as well as the number of reactivations or "spreads" in the ipso-and contralateral lung. There were 47 pneumonectomies and 33 lobectomies. Each procedure was complicated with four "spreads" or reactivations. No definite conclusions

can be drawn, however, from such a small and recently operated group of cases. Reversal of infectiousness occurred in 83.75 per cent of the entire group. Three

TABLE 12

Complications following pneumonectomy and lobectomy

	PNEUMONECTOMY (47 CASES)	LOBECTOMY (33 CASES)
Spread		
Ipsolateral	—	2
Contralateral	4	2
Dyspnea	1 (for 4 weeks)	1 (temporary)
Reactivation of other tuberculous foci	—	1 (middle ear) 1 (larynx)
Sinus of chest wall (tuberculous)	2	—
Ulceration of bronchial stump	2	—
Bronchopleural fistula	—	1 (with empyema, died) 1 (temporary)
Pleural effusion	2 (contralateral)	—
Wound infection	—	1 (osteomyelitis of rib stumps)
Hemothorax	1	—
Streptomycin reaction	1	1
Respiratory cripple	1	—

TABLE 13

Results in relation to indications (pneumonectomy and lobectomy)

	NUMBER	NEGATIVE		POSITIVE		DEAD
		Sanatorium	Home	Sanatorium	Home	
Thoracoplasty failure	41	21	12	5	—	3
Stenosis of bronchus	16	9	6	—	—	1
Bronchiectasis	8	5	1	1	—	1
Lower lobe lesions	4	3	1	—	—	—
Pneumothorax failure	4	3	—	1	—	—
Destroyed lung	3	1	1	1	—	—
Mistaken diagnosis	3	—	3	—	—	—
Tension cavity	1	—	1	—	—	—
Total	80 (100 per cent)	42 (52.5 per cent)	25 (31.25 per cent)	8 (10 per cent)	—	5 (6.25 per cent)

patients have died since leaving the hospital, but in only one of these was death due to tuberculosis. Two deaths occurred in older individuals. One was prob-

ably due to right heart failure while the other, which was sudden, was presumably the result of a myocardial infarction.

The duration of the state of noninfectiousness since operation is listed in table 15. As may be seen, 52 patients (65 per cent) are recorded in the "less than eighteen months" period. Fifteen (18.75 per cent) have remained noninfectious over periods of eighteen months to three years. As only 3 of the living patients

TABLE 14

Results of resection (all patients)

	NUMBER	REACTIVATION OR SPREAD		EXAMINATION OF SPUTUM FOR TUBERCLE BACILLI		DEAD
		Ipsolateral	Contralateral	Positive	Negative	
Pneumonectomy						
Right	18	—	2	2	15	1
Left	29	—	2	3	24	2
Lobectomy						
One lobe	21	2	2	2	18	1
Two lobes	11	—	—	1	9	1
Segmental	1	—	—	—	1	—
Total	80 (100 per cent)			8 (10 per cent)	67 (83.75 per cent)	5 (6.25 per cent)

TABLE 15

Duration of conversions since operation

	1 to 6 MONTHS	6 to 12 MONTHS	12 to 18 MONTHS	18 to 24 MONTHS	24 to 30 MONTHS	30 to 36 MONTHS	36 MONTHS
Thoracoplasty failure	7	7	6	6	1	4	1
Bronchostenosis	3	5	6	1	1	—	—
Bronchiectasis	2	3	—	—	—	—	1
Lower lobe lesion	1	1	2	—	—	—	—
Pneumothorax failure	1	2	—	—	—	—	—
Destroyed lung	1	—	1	—	—	—	—
Mistaken diagnosis	1	2	—	—	—	—	—
Tension cavity	—	—	1	—	—	—	—
	16	20	16	7	2	4	2

have shown "spread" or reactivation, it appears that not many complications should be expected in this group in the future. It is realized, however, that tuberculosis is an unpredictable disease and as time passes some of these apparently excellent results may eventually have to be classified as failures.

Streptomycin therapy prior to operation has been used in 26 of the 80 patients included in this group of pulmonary resections. The length of preoperative therapy has varied from four to one hundred and eighty days, but only 10 patients have had streptomycin for more than thirty-one days before surgery.

In these cases the indication for treatment was tuberculous endobronchitis. The control of their acute symptoms and the recognition of bronchostenosis led to the selection of pulmonary resection. In only 2 patients did the persistence of tuberculous bronchitis necessitate the prolongation of streptomycin for ninety to one hundred and thirty-six days. Three patients treated early in 1947 received 3.0 Gm. of streptomycin per day, one patient 2.0 Gm. per day, and three 1.5 Gm. per day. The remaining 19 patients received 1.0 Gm. per day.

With few exceptions, the 16 patients who were treated for less than thirty-one days were likewise treated because of bronchial disease. The bronchoscopic examination revealed bronchitis in most of these individuals, though there were several with upper lobe disease in which bronchial involvement, presumably tuberculous, was felt to be present from the findings on physical and roentgenologic examinations. Three patients with tuberculous empyema were treated for short periods preoperatively.

Streptomycin by the intramuscular route has been used postoperatively in 37 patients. The average length of treatment was for fourteen days with the usual dose of 1.0 Gm. per day.

From limited experience with streptomycin, the writers believe that it is of great value in the control of acute tuberculous bronchitis. Before the use of antibiotics these cases either had to be denied surgery or be operated upon at a considerably increased risk. A fair number of the group included under thoracoplasty failure had acute tuberculous bronchitis at the time of thoracoplasty. The bronchial lesion subsequently healed so that resection could be done.

In addition to the parenteral use of streptomycin in the postoperative period, the majority of the patients have received streptomycin as well as penicillin locally. The use of these drugs in lobectomies, where there must be constant postoperative closed drainage, has been limited to instillation in the wound at surgery. In postoperative pneumonectomies streptomycin and penicillin have been introduced into the pleural cavity at the time of aspirations until the fluid was well controlled or the space obliterated by thoracoplasty. The average length of such therapy was approximately ten days.

Experience with the postoperative group has been much too recent to attempt evaluation. Whether there will be any fewer late postoperative "spreads" or reactivation remains to be determined. In only one patient was it believed that a small contralateral "spread" occurred, although the lesion may have been atelectasis. This patient received streptomycin for twenty-six days and her course in the past nine months has been satisfactory. The gastric contents six weeks after surgery were negative for tubercle bacilli on culture.

The ideal length of postoperative streptomycin therapy is undetermined. The short period of therapy used in this series was selected arbitrarily. However, such a period of therapy is well worth evaluation. If "spill" to the other portion of the lung or lungs occurs, as seems likely, streptomycin should have an extremely beneficial effect. With this short period of treatment the phenomenon of streptomycin-resistance is less frequently encountered so that later spreads or reactivation might be benefitted by further treatment.

DISCUSSION

The choice of resection as a form of therapy came after several years of experience with other forms of collapse therapy. During the past ten years the writers have seen an increasing number of thoracoplasty failures and careful evaluation of these demonstrated that there were definite reasons for the failures. At times limited rib resection resulted in incomplete collapse after the first stage. Many of these were still ineffective after extensive revisions. Improperly selected cases were found to have been subjected to thoracoplasty before it was realized that the lesions were not suitable for this form of therapy. Large tension cavities at the apex, thick-walled cavities close to the mediastinum, high grade stenosis of the bronchus (often lobar) and bronchiectasis accounted for the major group of failures. The dictum that thoracoplasty should always be given first trial continued to be followed. Most patients showed improvement but the goal, that is, the elimination of tubercle bacilli, was not reached. The number of failures that accumulated as time passed, coupled with the newly developed surgical technique of individual ligation of the hilar structures with its associated low mortality, stimulated the writers to try to accomplish something for this discouraged group of patients. The availability of penicillin and streptomycin permitted operation on those patients who would have been refused for lack of a means of controlling ulcerative bronchitis. It now seems evident that thoracoplasty as previously used served only as a stopgap in the treatment of these cases.

The most frequent indication for resection in this series was thoracoplasty failure (41 cases). The next important indication was high grade bronchostenosis (16 cases). Various complications were also present in the form of hemoptysis, recurrent attacks of pneumonitis, sepsis and atelectasis. It was in the second group that the removal of the involved pulmonary tissue produced striking early results. The results in these two groups of cases have been most gratifying to date.

The remaining 30 per cent of the series presented individual problems as shown in the various tables. Most of these had received various therapeutic procedures before being considered for resection. A few cases were chosen for resection as the primary procedure because experience indicated that any other method would most likely fail.

Thoracoplasty was performed 26 times following resection. It is believed that this is advisable in all cases except those with lower lobe resection. In the more recent cases thoracoplasty was performed at the time of the resection if the patient's condition permitted, or as soon thereafter as possible. Following lobectomy, thoracoplasty ensures against over-expansion of the remaining lobe or lobes and should protect against ipsolateral reactivation. Thoracoplasty is equally important following pneumonectomy as it prevents a shift of the mediastinum with accompanying over-expansion of the contralateral lung and promotes early stabilization. Not infrequently tuberculous tissue is cut through during the operation and a thoracoplasty extensive enough to obliterate the dead space completely appears necessary if tuberculous empyema is to be avoided.

In several recent cases pneumonectomy has been performed in the presence of a tuberculous or mixed empyema and the infection controlled with frequent aspirations and the instillation of penicillin and streptomycin until a sufficiently adequate thoracoplasty could be done to obliterate the pleural space.

Phrenicotomy was originally performed following upper lobe lobectomy with the thought that reduction in the size of the pleural space would permit the remaining lobe to fill the space more quickly. It is now believed that phrenicotomy reduces the efficiency of the cough and promotes atelectasis. Thoracoplasty is done instead unless the lower lobe has been removed. In this instance phrenic section is used routinely as a substitute for thoracoplasty.

SUMMARY

Experience with 80 consecutive cases of pulmonary resection for tuberculosis is reported. The majority of these patients were failures with the usual collapse procedures and were doomed to continued sanatorium care because of persistent infectiousness.

Sixty-seven cases (83.75 per cent) of the entire group are noninfectious, 8 (10 per cent) still discharge tubercle bacilli and 5 (6.25 per cent) are dead. There were 2 operative deaths, yielding an operative mortality of 2.5 per cent.

A sufficient length of time has not passed to draw definite conclusions regarding the permanency of these results. If the cases follow the course reported by other authors, the satisfactory results will diminish with time. It must not be forgotten that tuberculosis is a systemic disease with many vagaries and that the removal of the symptom-producing focus is not the complete solution of the problem. Time has also shown that collapse therapy in the form of thoracoplasty has been found wanting under certain circumstances. Late spread and reactivation following thoracoplasty or resection should not be cited to condemn either procedure. Further experience with the methods at hand and newer methods may supply the answer.

Streptomycin when available was used before and after operation. It has proved most valuable in cases with acute ulcerative bronchitis. Many of the resections in the present series would have been ill advised and dangerous before streptomycin was available. The drug is given in doses of 1.0 Gm. daily. Frequent instillations into the pleural cavity following pneumonectomy have prevented the common complication of tuberculous empyema until the space was obliterated. It is believed that chemotherapy is partially responsible for the low number of reactivations and "spreads" and that it has helped to control them once they have occurred. Penicillin has been used extensively throughout the series.

SUMARIO

La Resección Pulmonar en el Tratamiento de la Tuberculosis

Comunícase lo observado en 80 casos consecutivos de resección pulmonar por tuberculosis. La mayoría de los enfermos representaban fracasos de los habituales procedimientos de colapso y estaban condenados a continua asistencia sanatorial debido a su infecciosidad persistente.

Sesenta y siete casos (83.75 por ciento) del grupo total ya no son infecciosos, 8 (10 por ciento) todavía expulsan bacilos tuberculosos y 5 (6.25 por ciento) han muerto. Hubo 2 muertes quirúrgicas, dando una mortalidad operatoria de 2.5 por ciento.

No ha trascurrido aun suficiente tiempo para poder sacar conclusiones definitivas acerca de la permanencia de los resultados. Si los casos se conforman al patrón presentado por otros autores, los resultados satisfactorios irán disminuyendo con el tiempo. No hay que olvidar que la tuberculosis es una enfermedad orgánica y bastante caprichosa y que la eliminación del foco sintomatógeno no representa la solución completa del problema. El tiempo también ha revelado que la colapsoterapia en forma de toracoplastia ha resultado deficiente en ciertas circunstancias. No deben citarse la difusión y reactivación tardias después de la toracoplastia o la resección para condenar uno u otro procedimiento. Nuevas tentativas con las técnicas disponibles y con otras más nuevas tal vez faciliten la respuesta.

La estreptomicina, cuando la había, fué utilizada antes y después de la intervención, resultando más valiosa en los casos con bronquitis ulcerada aguda. En la serie actual, muchas de las resecciones hubieran sido indiscretas y peligrosas antes de contarse con la estreptomicina. La droga fué administrada a dosis de 1 Gm. diario. Las frecuentes instilaciones en la cavidad pleural consecutivamente a la neumectomía han impedido las habituales complicaciones del empiema tuberculoso hasta la obliteración del espacio. La quimioterapia parece ser en parte la causa del pequeño número de reactivaciones y "difusiones" y también parece haber ayudado a cohibirlas, una vez aparecidas. La penicilina fué empleada en gran escala en toda la serie.

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DECORTICATION OF THE LUNG IN PATIENTS WITH PULMONARY TUBERCULOSIS[1, 2]

PAUL V. O'ROURKE, E. J. O'BRIEN, AND WM. L. TUTTLE

INTRODUCTION

The results during World War II of decortication of the lung in the management of organizing hemothorax are well known and accepted. Some thoracic surgeons hoped that this technique could be applied successfully in certain tuberculous patients with a persistent pleural space in whom conservative measures had failed. This hope was based on the belief that the thickened pleura seen in those cases of tuberculosis was in reality a fairly normal visceral pleura covered by an organized exudate or "peel" similar in many ways to that seen in organizing hemothorax. Fear had been expressed that the "peel" could not be removed from the visceral pleura because of its firm adherence; that the complications occurring from its removal, if possible, would be very great; and that tuberculous wound infections and failure to obliterate the pleural space would occur frequently enough to exclude its common usage.

This study was undertaken by the writers who are fully aware of these possibilities but anxious to learn if decortication is surgically feasible in tuberculosis. It consists of 43 cases of pulmonary and pleural tuberculosis decorticated between January 1946 and May 1948. There were 30 males and 13 females; 38 were white and 5 were Negroes.

INDICATIONS FOR DECORTICATION

For the most part only patients with complications of tuberculous pleurisy with effusion or pneumothorax were considered for this operation. It was used also as an adjunct to lobectomy when the need arose. The indications for decortication in the group having tuberculous pleurisy with effusion have been restricted to those patients in whom: (a) the fluid became organized or loculated and could no longer be removed by aspiration; or (b) the fluid had been aspirated and replaced by air resulting in an unexpandable lung. As shown in table 1, there were 9 cases in this group. In 2 of the 5 patients with loculated fluid which failed to respond to aspiration a positive diagnosis of pleural tuberculosis was not made preoperatively, but was made histologically from the "peel." Of the 2 patients with tuberculous empyema, one occurred in the youngest patient, four years old, who had been a contact of his mother before she was discovered to have tuberculosis (figure 1). In the patient with a mixed empyema the process began as a tuberculous pleural effusion, which was aspirated for two years with little benefit. After a routine aspiration, the patient developed fever and the

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[2] Presented before the Medical Section, as part of the *Symposium on Surgery—Trends—Late Results*, at the 44th Annual Meeting of the National Tuberculosis Association, New York, New York, June 16, 1948.

TABLE 1

Indications for decortication

	NUMBER OF PATIENTS	
I. Complications of Tuberculous Pleurisy		
a. Unexpandable lung	1	
b. Mixed empyema with unexpandable lung	1	
c. Tuberculous empyema with unexpandable lung	2	
d. Loculated fluid with unexpandable lung	5	
Total		9
II. Complications of Pneumothorax		
a. Unexpandable lung	3	
b. Mixed empyema with unexpandable lung	3	
c. Tuberculous empyema with unexpandable lung	7	
d. Pleural effusion with unexpandable lung	14	
Total		27
III. Adjunct to lobectomy	7	7
Total		43

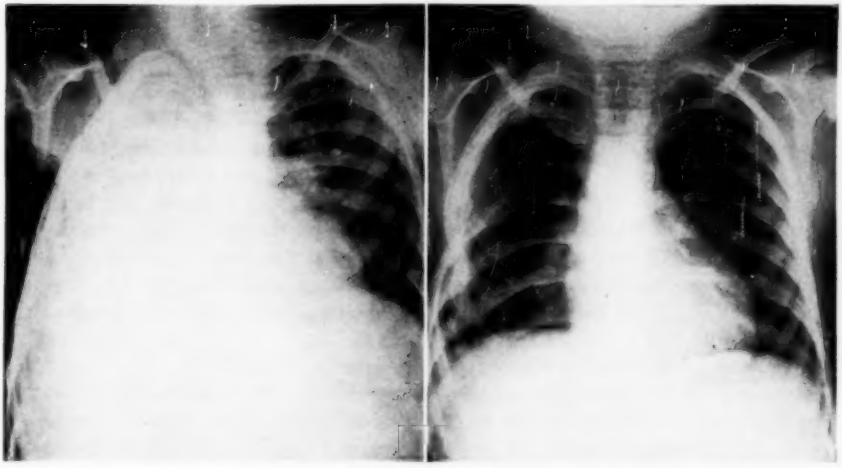

FIG. 1a. (Left) Preoperative film dated March 6, 1948. Age 4 years. Tuberculous pleurisy with empyema.

FIG. 1b. (Right) Postoperative film dated May 10, 1948. Decortication done March 15, 1948.

fluid, which had always been clear, became purulent. *Staphylococcus aureus* was recovered upon culture of the fluid from the pleural cavity. The infection was immediately drained. One year after the drainage, because of the persistent

pleural space, a decortication was done successfully. Re-expansion of the lung at the end of the operation was good but postoperatively the expansion was not sustained.

The second indication used by the writers have been the complications which accompany or follow therapeutic pneumothorax, such as troublesome fluid or empyema occurring during the program of pneumothorax, or failure of the lung to re-expand after pneumothorax had been abandoned. There were 27 patients in this group. Ten patients had tuberculous or mixed empyema which failed to respond to pleural lavage and the lung remained collapsed after aspiration of air or fluid. There were 14 patients with pleural effusion occurring during the re-expansion program or during the period of the therapeutic pneumothorax, in which the lung failed to re-expand after aspiration and discontinuance of air refills. This is the largest single group for which a decortication has been performed. The encased or unexpandable lung without fluid has been decorticated in three instances to obliterate the pleural space and to prevent shift of the mediastinum and over-distention of the contralateral lung. In the beginning this particular indication was used hesitantly because most of these patients were at home and apparently doing well. It seemed inadvisable to change an apparently satisfactory program until it was apparent that decortication could be done with relative safety. In 2 of the 3 cases in this group the indications for decortications were impelling. One, a woman who had been receiving pneumothorax refills for six years, had some bleeding into the pleural space with the formation of a large clot following a refill of air. The pleura above the clot showed thickening on the roentgenogram and re-expansion of the lung seemed unlikely unless a decortication could be done. After the clot had been removed the lung would not re-expand even though positive pressure was applied through an intratracheal tube. A decortication was done easily and complete re-expansion was obtained (figure 2). The second patient was a doctor engaged in tuberculosis work who had been observing the results of the study and requested a decortication of his unexpanded lung. His wishes were finally granted and an excellent result was obtained. As the encased lung without fluid seems to represent one of the better indications, it is planned to use it with increasing frequency in the future.

The third indication is represented by a group of 7 patients upon whom a lobectomy was performed and a "peel" removed from the remaining lobes to aid in their re-expansion and to hasten obliteration of the pleural space. Incidentally, in 3 pneumonectomies not included in this series a decortication was first done to facilitate the indentification and handling of the hilar structures.

The duration of the pneumothorax, as listed in table 2, has varied from four months to sixteen years and in five instances has been present for ten years. Ability to separate the "peel" from the visceral pleura does not seem to be related to the duration of the pneumothorax *per se* but rather to the amount and extent of the peripheral pulmonary disease.

Unless some emergency arose requiring surgical intervention, an adequate trial of re-expansion was attempted and only when further efforts seemed hazardous or futile was decortication employed.

A complete decortication was not always possible or desirable, because of the underlying disease, nor always necessary because of the small size of the remaining

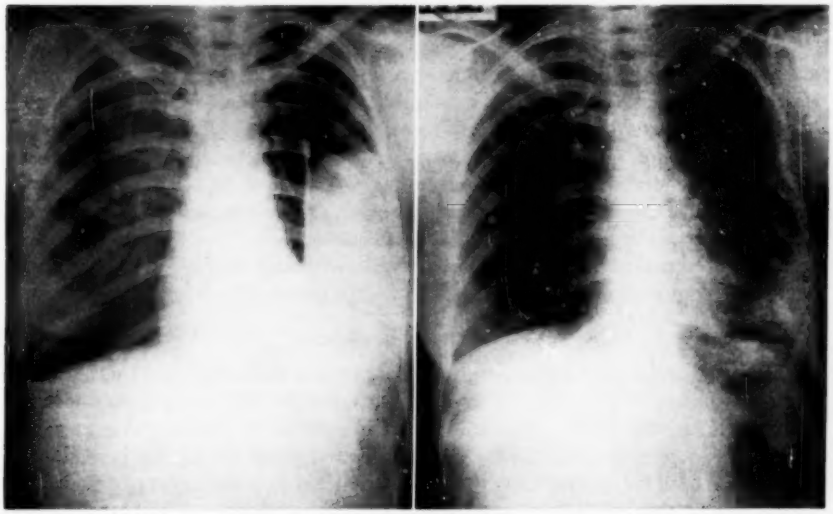

FIG. 2a (Left) Preoperative film dated September 18, 1947. Duration of pneumothorax six years. Bleeding and formation of clot following refill.

FIG. 2b (Right) Postoperative film dated April 19, 1948. Decortication done September 22, 1947.

TABLE 2

Duration of pneumothorax

	NUMBER OF PATIENTS
Less than one year	4
Two years	5
Three years	4
Five years	3
Six years	2
Seven years	1
Eight years	1
Ten years	5
Fourteen years	1
Sixteen years	1
Total	27

pleural space. Twenty-eight lungs were completely decorticated and 15 partially. Early in the study it was observed that a lobe containing considerable fibrosis as a result of previous disease did not re-expand well even though it was completely decorticated. Since then, if the disease-free lobes after decortication

filled the hemithorax, no attempt has been made to remove the "peel" from the lobe which was the site of the major disease. Perhaps it is better to keep the diseased lobe permanently collapsed than risk the danger of reactivation from re-expansion.

The majority of patients in this series were subjected to the operation without streptomycin as an adjunct because it was not available. More recently, however, streptomycin has been used in 19 instances either because of complications encountered at operation, such as subpleural tubercles, or to prepare the patient for the procedure. It is believed at present that practically all individuals should receive streptomycin as a routine procedure if for no other reason than prophylaxis. It should be emphasized, however, that the paramount consideration for success is dependent upon adequate removal of the "peel" without undue trauma to the underlying lung. That streptomycin may improve the result and hasten the convalescence seems indicated but it is no substitute for good surgery.

TECHNIQUE OF OPERATION

The actual technique of the operation did not differ from that used by thoracic surgeons during World War II in the treatment of organizing hemothorax. All operations were done with intratracheal anesthesia of nitrous oxide-oxygen and ether. Approximately 1,500 cc. of blood were given during the procedure. Cotton was used for ligatures and wound closure. In most instances one medium sized rubber tube drain was placed dependently just above the diaphragm in the posterior axillary line and a smaller tube was inserted high anteriorly to allow for the escape of air. Both tubes were connected to water-sealed bottles.

The immediate postoperative course did not differ from that of the usual patient with tuberculosis undergoing surgery. Fever was not excessive or prolonged except in the one patient who died three months after operation from disseminated tuberculosis. Two patients needed bronchoscopy to remove retained bronchial secretions.

As soon as the amount of drainage stopped fluctuating, the tubes were removed. The tubes were withdrawn, on an average, by the fifth day in 31 cases. If fluoroscopy or roentgenograms showed the presence of loculated fluid or trapped air, they were removed by aspiration. Nine patients required frequent thoracentesis over a period of several weeks. During the time of re-expansion they were watched very closely and every effort was made to keep the pleural space dry and as free from trapped air as possible. Deep breathing exercises were started as soon as the tubes were removed and were continued indefinitely.

COMPLICATIONS

In 5 patients there were seven complications attributable to the operation, as shown in table 3. One patient with pleural tuberculosis and empyema did non re-expand at the completion of the operation despite the successful removal of a "peel". In 3 additional patients a partially successful decortication was done and the immediate re-expansion of the lung seemed good when positive

pressure was used. Complete re-expansion was not sustained, however, during the postoperative period. Two of the latter have had a thoracoplasty performed which obliterated the pleural space and they are now at home.

At the time of operation it was not infrequent that small bubbling air leaks were seen. In all but 3 instances these were not of any consequence and apparently sealed off within a few hours. Of the 3 patients in whom air leakage continued, 2 developed mixed empyema and were drained. In one patient the fistula closed soon after drainage. In the other, the fistula has remained open and the prognosis is unfavorable. The third instance of bronchial fistula was

TABLE 3

Immediate postoperative complications

	OCCURRENCE*
Expansion of lung not sustained	3
Nonexpansion of lung	1
Bronchial pleural fistula with mixed empyema	2
Bronchial pleural fistula (only)	1
	–
Total	7

* The seven complications occurred in a total of 5 patients.

TABLE 4

Late complications of disease

	OCCURRENCE	NUMBER OF PATIENTS
Positive sputum (only)	2	2
Bilateral reactivation	1	1
Disseminated tuberculosis (death)	1	1
Incisional sinus infection only (4 months)	1	1
	–	–
Total	5	5

uncomplicated by infection. In this case a posterior thoracotomy tube was converted to an open drainage tube and the space gradually obliterated and the fistula closed.

In 5 patients there were late complications, as listed in table 4. Two developed sputum positive for tubercle bacilli. In another patient a single culture positive for tubercle bacilli was obtained within one month of operation. This patient later "converted" and she has remained noninfectious. The other patient ultimately "converted" and has been noninfectious for eleven months. In neither was there roentgenological evidence of reactivation nor was other therapy except bed-rest added to influence the bacteriologic status. One patient had bilateral reactivation of disease with reopening of cavity in the ipsilateral lung. This was the only instance in the entire series of a previously closed cavity reopening after

the procedure. This patient probably contributed to his own breakdown because of leaving the hospital against advice. He was later readmitted with evident spread of his disease. One patient had widespread dissemination of disease resulting in ultimate death. This patient was a colored male who originally had bilateral disease and developed a tuberculous empyema as a complication of pneumothorax. The decortication was not difficult and re-expansion was very good at the end of the operation. The expansion was not sustained, however, and his course was one of steady progression of the disease. This resulted in death three months after operation. Streptomycin might have altered the course of his disease but it was not available when his operation was performed.

RESULTS

The results of decortication of the lung in patients with tuberculosis have been evaluated in this series by ability to obliterate the persistent pleural space. If this objective can be obtained, it justifies the procedure in most instances because it lessens the chance of the existing pleural space becoming infected. Also it prevents emphysema developing in the contralateral lung as a result of the mediastinum shifting to aid in obliterating the pleural space. This occurs when most pneumothoraces are discontinued and an effort is made to re-expand the lung. Although patients have voluntarily stated that their breathing was improved after the operation, this may not mean that there has been any restoration of pulmonary function. Even though the pulmonary bed has been increased in size, the ability to exchange oxygen may not have been improved and the amount of unoxygenated blood may be increased.

TABLE 5

*Results of decortication**

	NUMBER OF PATIENTS
Failure	4
Improved	5
Good	14
Excellent	20
Total	43

* In an additional 4 patients decortication could not be performed.

There were 4 patients in whom expansion of the lung was not sustained and they have been classified as failures of operation.

If the pleural space was entirely obliterated and the lung appeared to be fully aerated, this has been classified as an excellent result. There were 20 patients in this category including the 7 lobectomies.

If the space was obliterated but shadows were present indicative of incomplete re-expansion of the lung, the result has been classified as good. In this group there were 14 patients.

If there was increased aeration of the lung and the pleural space was smaller, the result was listed as improved. In this group there were 5 patients.

In 4 additional patients, not included in this series, a decortication was attempted but the "peel" could not be separated from the visceral pleura and it was necessary to do a thoracoplasty.

It will be noted by referring to table 6 that of the 43 patients operated upon, 31 are well and at home. Eleven patients are still in the hospital. Four of this group are ready for discharge and 4 have been recently operated upon and are progressing satisfactorily. One patient developed a tuberculous wound sinus but this is healing. Two are resident in the hospital because of poor progress; one with a bilateral reactivation of disease and the other with a bronchial pleural fistula and mixed empyema. The ultimate outcome of the latter patient is most uncertain.

TABLE 6

Present status

	NUMBER OF PATIENTS
At home	31
In hospital	11
Dead	1
Total	43

SUMMARY

1. The lungs of 43 patients with tuberculosis have been decorticated successfully, thereby demonstrating the presence of a "peel" similar to the organized exudate found encasing the lung in organizing hemothorax. In 4 additional patients decortication was not technically feasible.

2. The indications for decortication have been restricted to the complications of tuberculous pleurisy in 9 patients and the complications of therapeutic pneumothorax in 27 patients. In addition, 7 patients were decorticated in conjunction with a lobectomy.

3. The success or failure to remove a "peel" does not seem to be related to the duration of the pneumothorax but rather to the amount of the peripheral pulmonary disease.

4. Twenty-eight lungs were completely decorticated and in fifteen a partial decortication was performed.

5. Streptomycin was not available at the beginning of this study but since becoming more plentiful has been used routinely.

6. The immediate postoperative complications were: nonexpansion of the lung, expansion not sustained, and bronchial pleural fistula with or without mixed empyema.

7. The late complications of disease were: positive sputum only, 2 patients; bilateral reactivation of disease with reopening of cavity in the decorticated

lung, one patient; tuberculous incisional sinus infection, one patient; and disseminated tuberculosis with ultimate death, one patient.

8. The results of decortication in the 43 patients have been classified as: failure, 4; improved, 5; good, 14; and excellent, 20. The effect on pulmonary function is discussed.

9. The present status of the patients is as follows: 31 at home, 11 in hospital, and one dead.

CONCLUSIONS

Decortication is a valuable adjunct to the armamentarium for the treatment of pulmonary and pleural tuberculosis. The results obtained warrant its continued usage, accompanied by further investigations of the respiratory function of the decorticated lung.

SUMARIO

La Decorticación del Pulmón en los Tuberculosos Pulmonares

1. Los pulmones de 43 tuberculosos fueron decorticados con éxito, demostrando así la presencia de una "cápsula" semejante al exudado organizado que encierra el pulmón en el hemotórax organizado. En otros 4 enfermos la decorticación no resultó técnicamente factible.

2. Las indicaciones de la decorticación fueron limitadas a las complicaciones de la pleuresía tuberculosa en 9 enfermos y a las del neumotórax terapéutico en 27. Además, 7 enfermos fueron decorticados en relación con una lobectomía.

3. El éxito o fracaso en la separación de la "capsula" no parece guardar relación con la duración del neumotórax, sino más bien con la extensión de la neumopatía periférica.

4. En 38 pulmones la decorticación fué total y en 15 parcial.

5. Al comienzo del estudio no había estreptomicina a mano, pero desde que ha sido más obtenible, se ha empleado sistemáticamente.

6. Las inmediatas complicaciones postoperatorias fueron: inexpansión del pulmón, expansión insostenida, y fístula pleurobronquial con o sin empiema mixto.

7. Las complicaciones tardías de la enfermedad fueron: solamente esputo positivo, 2 enfermos; reactivación bilateral de la dolencia con reapertura de la caverna en el pulmón decorticado, 1 enfermo; infección tuberculosa de la fístula incisional, 1 enfermo; y granulia culminando en la muerte, 1 enfermo.

8. El resultado de la decorticación en los 43 enfermos fué clasificado así: fracaso, 4; mejoría, 5; bueno, 14; y excelente, 20. También se discute el efecto sobre la función pulmonar.

9. El estado actual de los enfermos es éste: 31 en sus casas, 11 en el hospital, y uno ha muerto.

CONCLUSIONES

La decorticación constituye una valiosa adición al arsenal dedicado al tratamiento de la tuberculosis pulmonar y pleural. El resultado obtenido justifica la continuación de su empleo, junto con nuevas investigaciones de la función respiratoria del pulmón decorticado.

PULMONARY TUBERCULOSIS INVOLVING THE LOWER LOBES[1, 2]

EMIL ROTHSTEIN

INTRODUCTION

Pulmonary tuberculosis involving the lower lobes is a phenomenon of recognized occurrence and is sufficiently common to warrant consideration as a diagnostic problem in every lower lobe pulmonary lesion.

Because of its location, lower lobe tuberculosis presents definite problems in diagnosis and treatment which are different in certain ways from those encountered in upper lobe disease. In addition, there has recently arisen an immunologic problem in the pathogenesis of lower lobe disease, suggested by the work of Dr. William Dock (1). The present study was attempted in an effort to explore these problems.

Definition

In this study the following types of lesions have been observed: (*a*) all cases with the chief or only lesion immediately above the diaphragmatic shadow; (*b*) all cases with the chief or only lesion in the lower one-half of the lung fields when by appropriate lateral or oblique views these were demonstrated to lie within the anatomical boundaries of either lower lobe. Cases in which extension or spread to the lower lobe occurred from known pre-existing upper lobe disease have not been included. In each case the first roentgenogram, at least, showed the lower lobe involved and the upper lung fields essentially clear. In addition, bacteriologic proof of the tuberculous etiology has been obtained in each case.

OBSERVATIONS

Forty-eight cases of lower lobe tuberculosis have been studied from the patient population of the U. S. Veterans Administration Hospital, Wood, Wisconsin. This service is a tuberculosis unit of 430 beds. The cases have been observed for an average period of three years. No effort was made to calculate the percentage of lower lobe disease as the cases were not chosen from consecutive admissions.

Incidence: All but one of the patients were males. It is recognized (2, 3) that lower lobe tuberculosis is more common in females but there is no regular tuberculosis service for female patients at Wood. The average age of the patients was 32 years while the age of a control group was 41. This incidence of lower lobe disease in a younger age group has been found by various other investigators as well. Six infections were in Negroes.

[1] From the U. S. Veterans Administration Hospital, Tuberculosis Division, Wood, Wisconsin.

[2] Published with permission of the Chief Medical Director, Department of Medicine and Surgery, Veterans Administration, who assumes no responsibility for the opinions expressed or conclusions drawn by the author.

Diagnosis and Cause of Illness

Although lower lobe tuberculosis is fairly common, it still does not receive the attention it deserves from the standpoint of diagnosis. Of the total group, 24, or one-half, presented initial difficulties in diagnosis. This led to delayed recognition of from a few weeks or months to several years. In most delayed diagnoses in tuberculosis patients the error lies in failing to obtain chest roentgenograms, but in lower lobe disease the delay may occur despite positive roentgenologic findings. The most common error in this regard was to consider an infiltrative lesion as nontuberculous despite suggestive evidence of cavitation in some instances. Frequently this resulted in the return of the patient to duty or his discharge from the hospital while the chest roentgenograms still revealed definite disease. Because of its location, the lesion was usually considered as an unresolved or slowly resolving nontuberculous "virus" pneumonitis and was apparently thought to be of little ultimate significance. In several cases bronchoscopy and bronchography were performed because of a suspicion of bronchiectasis or new growth. In two cases neoplasm could not be excluded despite considerable study and resection was performed. Another reason for failure to diagnose lower lobe tuberculosis is the frequency of lesions, usually cavitary, which are in the apex of a lobe. On the usual postero-anterior film these lesions may be projected into the hilar shadow. This is an area where annular shadows of vascular origin are common, and small cavities here are relatively easily overlooked. In a few instances the lesion was partly or entirely hidden by the heart shadow. In one case a 4 cm. cavity was so completely obscured by the heart as to permit a postero-anterior film to be interpreted as normal except for some cardiac shift to the left. In a number of cases in which the diagnosis was overlooked, the patient returned to medical observation only after considerable extension of the disease had occurred; in several instances this was severe enough to make recovery impossible.

Extent and distribution of lesions: Of the entire group only 2 were minimal at the time of admission to Wood; 24, or 50 per cent, were moderately advanced and the remainder far advanced. This overwhelming incidence of advanced disease would not have been unusual in a prewar series of routine hospital admissions for tuberculosis. The situation has been considerably changed, however, as a result of the use of chest roentgenograms as a part of routine examinations in the service. Consequently, if every tuberculous lesion were diagnosed on the first film, it would be anticipated that the percentage of minimal lesions would be high. The reason this is not the case with lower lobe lesions may be explained by the fact that 5 cases which were minimal on the first roentgenographic examination were moderately or far advanced upon first diagnosis. Others of this series were diagnosed as "pneumonia" months before the presence of tuberculosis was recognized. In many such instances it is reasonable to assume that lower lobe physical signs, in the absence of a roentgenogram, led to an appreciable delay in arriving at the correct diagnosis.

An analysis of the anatomical distributions and characteristics of these lesions revealed that 30, or 60 per cent, were at the apex of the right or the left lower lobe

and most of these were so-called hilar cavities; the remainder were in the basal portion of the lower lobes. Twenty per cent of the lesions were predominantly infiltrative, 60 per cent cavitary and 18 per cent pneumonic. In one case the lesion could be classified as a tuberculoma. Lateral views of the "hilar" cavities were especially interesting and almost always showed the lesions to be posterior, overlying the vertebral bodies. Figures 1 and 2 show an unusually large lower lobe cavity and its posterior location.

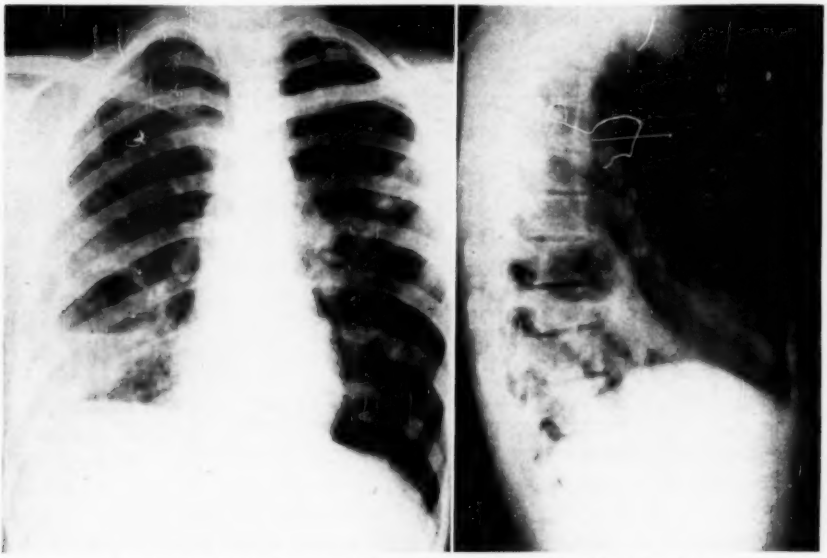

FIG. 1. (Left) Illustrating large right lower lobe cavity. Note fluid level. Sputum repeatedly positive for tubercle bacilli.

FIG. 2. (Right) Lateral film of same patient. Illustrated are the posterior position of the lesion, the fluid level and the surrounding atelectasis of the dorsal segment in the lower lobe.

In addition to lateral views, oblique projections were especially valuable in demonstrating retrocardiac lesions. Here special use was made of a left anterior oblique film taken from 5 to 10 degrees from the postero-anterior axis. At this small angle the left cardiac border is superimposed on the left side of the spine while the retrocardiac lung field, including the entire left lower lobe, is thrown into clear vision. This view has certain advantages over the direct lateral or standard left oblique view because in these two positions a thin-walled cavity may be superimposed upon the spine and fail to be visualized for lack of sufficient density. The accompanying diagrams (figures 3, 4, and 5) illustrate this phenomenon. With this method, as with all special projections, the preliminary use of fluoroscopy is of great value. The lesions were distributed approximately equally between the right and left lungs and two were bilateral at the time of discovery.

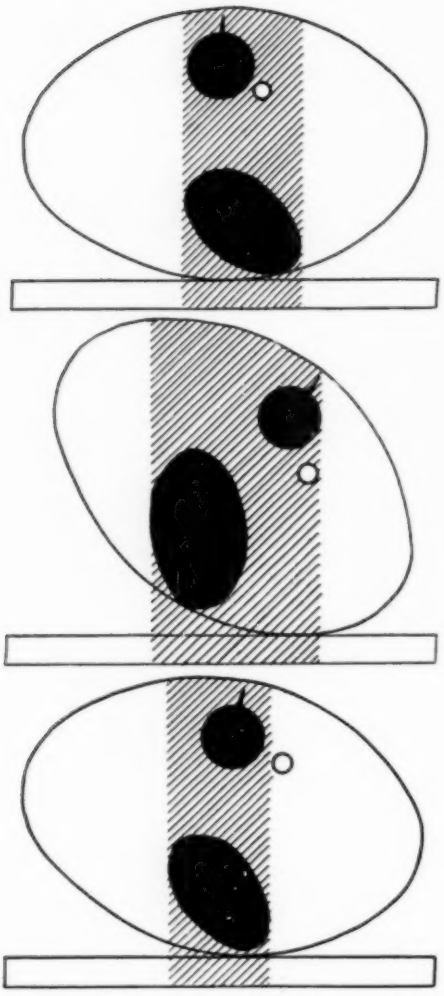

FIG. 3. (Top) Illustrating how a cavity situated in the apex of the left lower lobe may be hidden by the cardiac shadow on the P.A. projection.

FIG. 4. (Center) Illustrating how the same cavity may be hidden by the shadow of the spine in the usual left oblique projection.

FIG. 5. (Bottom) The cavity can be visualized by means of a left oblique film made about 15 degrees from the P.A.

Bronchial disease: An interesting observation, and one with diagnostic and therapeutic significance, was the high percentage of bronchial disease. The presence of any one of the following three criteria was accepted as diagnostic of sig-

nificant bronchial involvement: (*1*) bronchoscopic evidence of stenosis or severe tracheobronchitis: (*2*) roentgenographic evidence of atelectasis before collapse therapy or immediately after induction of pneumothorax; or (*3*) cavity behavior characteristic of a tension cavity.

Bronchial disease was believed to be present in 37 patients (75 per cent). Well over one-half of these had typical tension cavities, while 25 per cent each showed atelectasis or bronchoscopic findings. Many cases showed two or all three of these evidences of bronchial tuberculosis. The relatively small number of positive bronchoscopies was due in part to the fact that many patients were not bronchoscoped. Moreover, the distal bronchi only may have been involved and these would often be inaccessible to the bronchoscope. In a series of 50 patients admitted consecutively with disease in the upper lobes, the incidence of bronchial disease was considerably lower (7 cases) than in the lower lobe cases.

Clinical course: During the period of study many (60 per cent) of the lower lobe lesions showed evidences of extension. In most instances the extensions were to the upper lobes and were roentgenologically similar in appearance and in behavior to "spreads" found in primarily upper lobe cases. In a fair proportion the "spread" had occurred at the time of the first diagnosis, although earlier films in each case were available showing that the disease was primarily lower lobe at its start. In some, the "spreads" occurred within a few weeks of diagnosis while in others many years elapsed during which time the lesion remained confined to the lower lobe.

Prognosis: The average period of observation of the group was three years. It appears that the outlook for these lesions even to the point of arrest is only fair. Long term (2 to 5 years) follow-ups are not available in any of these inactive cases. Nevertheless, of the total number, 5 are dead, 19 are arrested, and the remainder are active. Some of the last named group are on the road to arrest while others will undoubtedly fail to recover. In this study the diagnosis of "arrested" was made by the most rigid criteria, *i.e.*, stable roentgenographic findings compatible with a healed lesion for well over the minimum of six months, numerous negative examinations for tubercle bacilli, including sputum and gastric cultures, and four to six months of walking exercise. It is understood and emphasized, however, that "arrest" in a previously cavitary lesion is not synonymous with "cure." Many upper lobe cavitary lesions "arrest" with subsequent relapse. Such instances are usually from a group who were treated with either no collapse measures or collapse therapy of only short duration. Since these lower lobe cases, by and large, became arrested by the aid of similar short term collapse measures, a very cautious attitude should be maintained as to the ultimate fate of these patients.

Treatment

No one form of treatment has proved eminently satisfactory and this study did not reveal the ideal treatment for lower lobe tuberculosis. These patients have had almost the entire spectrum of therapeutic measures that are applied by the phthisiologist.

Pneumothorax: Sixteen patients had artificial pneumothorax on the side of the lower lobe lesion. The results were bad in every case. They will be detailed in another report (4) but were characterized by atelectases, pleural effusions, unexpandable lungs, and persistently open cavities. In not a single case could pneumothorax be carried as a "clean" satisfactory collapse for two to three years with satisfactory re-expansion of the lung and eventual arrest of the disease.

Resection: Three patients were subjected to resection procedures. In 2 the diagnosis of neoplasm could not be excluded. In one patient the disease became arrested after lobectomy and in the other a similar result was observed after pneumonectomy. In the latter patient, however, extrapulmonary lesions appeared which are gradually responding to streptomycin and orthopedic surgery. The third resection, a lobectomy, was done in a patient who had attained an unsatisfactory result despite various combinations of phrenic surgery, pneumoperitoneum, pneumothorax, and streptomycin. A postoperative spread of disease to the other lung occurred and the ultimate prognosis does not seem favorable.

Thoracoplasty: Thoracoplasty was not used as a treatment for any lesion limited to a lower lobe. The operation was performed in 4 patients for the following indications: unexpandable lung (postpneumothorax), extensive ipsolateral upper lobe extension, contralateral upper lobe extension, and following pneumonectomy. In 3 of these patients the disease is arrested and in the fourth it is still active.

Cavernostomy: In 2 patients open cavernostomies have been performed through the posterior chest wall. In one case streptomycin plus surgery led to temporary cavity closure, and in the other cavernostomy was combined with one month of streptomycin followed by phrenic surgery and pneumoperitoneum. It is too soon to evaluate the treatment.

Streptomycin: Six cases received bed-rest plus streptomycin, unaccompanied by surgery. Two were treated for extensive "spreads" and died during treatment. Three, with tension cavities and "spreads", showed slight but insignificant improvement. In one patient the disease became arrested.

Phrenic nerve crush: Phrenic surgery was performed alone in 4 cases. It was combined with pneumoperitoneum in 13 cases and with pneumothorax in 5. Of those with phrenic crush alone, the disease remained active in one and became arrested in 3. With the combination of phrenic crush and pneumoperitoneum the disease became arrested in 7 and is still active in 6 patients. Phrenic surgery plus pneumothorax resulted in three arrested lesions while two remain active. In each case where phrenic surgery with or without pneumoperitoneum was effective, cavity closure occurred early (three to six months) with reversal of infectiousness and clearing of exudative lesions. Pneumoperitoneum in this group was continued for an average of two and one-fourth years. The optimum duration of this treatment is not known and only observation of this type of case for five or more years will reveal whether this period of pneumoperitoneum (two and a quarter years) is long enough to promote permanent healing. At the present time there must be considerable doubt about the permanence of healing of a large cavity with surrounding disease, in the absence of permanent collapse of the lung

area involved, despite early good results. Figures 6 and 7 illustrate a spectacularly successful result with phrenic surgery and pneumoperitoneum in the patient whose initial films are shown in figures 1 and 2.

Rest treatment: Twelve patients received bed-rest only. In 7 the lesions were still confined to the lower lobes when this treatment was started. Of these there were 5 good results (the basal lesion cleared or became inactive, although one required contralateral thoracoplasty for an extension of the disease) while 2 have remaining active lower lobe disease. Spontaneous cavity closure occurred in 3 of these 5 patients with good results, and clearing of the infiltrate occurred in the

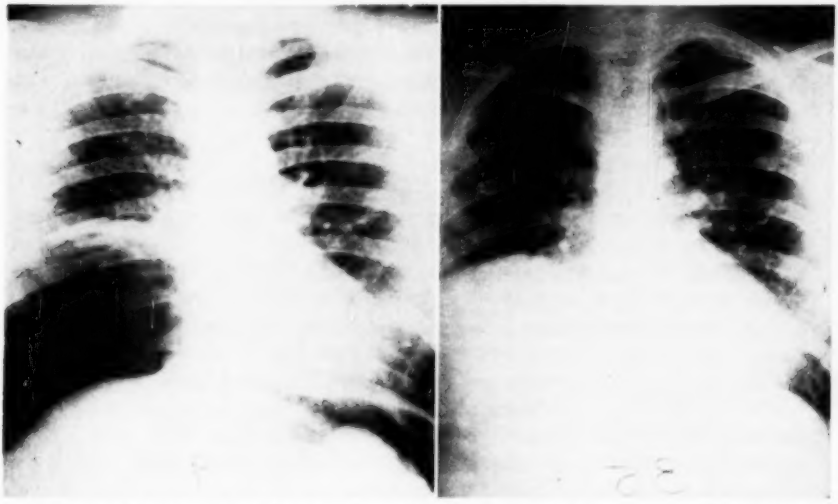

FIG. 6. (Left) Result with phrenic crush and pneumoperitoneum. Same patient as shown in figures 1 and 2, three years later. Sputum and gastric washings are repeatedly negative for tubercle bacilli on culture.

FIG. 7. (Right) Same case shown in figures 1, 2 and 6. Disease arrested with pneumoperitoneum abandoned after two and one-half years.

others. Such behavior is not uncommon with tension cavities, due perhaps to complete occlusion of the draining bronchus.

In summarizing the results of treatment these patients must be divided into two groups. One consists of those individuals who originally had lower lobe disease but in whom the disease has spread to such a point that treatment directed towards lower lobe tuberculosis could no longer be evaluated. The remainder (35 patients) had lesions confined to the lower lobe while undergoing treatment. By "good" results here are meant: (a) arrested tuberculosis, or (b) an inactive lesion on the lower lobe side despite continuing active contralateral upper lobe disease. The latter category was included as it is felt that lower lobe tuberculosis presents a mechanical as well as an immunological problem in cavity closure.

Rest alone was used in 7 cases, with good results in 5. Rest plus streptomycin gave good results in one case with poor results in 3 others. Phrenic crush alone yielded good results in 3 and poor in none. The results observed with phrenic crush plus pneumoperitoneum were good in 8 instances and poor in 3. Pneumothorax gave poor results in 13 patients and questionable results in 3 others. Pulmonary resection yielded good results in 2 cases and was of doubtful value in a third, and cavernostomy was followed by one good and one fair result. It may be seen from these figures that there is no "ideal" treatment plan revealed by study of this series but the observations point to certain tentative conclusions: (1) pneumothorax is contraindicated in this type of lesion; (2) rest, probably supplemented at an early date by phrenic nerve crush and pneumoperitoneum, offers the best chance of reaching arrest with relatively conservative measures; and (3) cavernostomy (with or without phrenic crush and pneumoperitoneum) and resections, supplemented by streptomycin, should be held in reserve until the above measures are unsuccessful.

Possible Relationship of Location of Lesion to Resistance to Tuberculosis

One question toward which this study was directed bears on the pathogenesis of lower lobe tuberculosis, in view of Dock's theory of upper lobe localization of this disease. In a carefully calculated mathematical demonstration, Dock has utilized newer knowledge of cardiovascular dynamics to prove that the circulation in the pulmonary apices is virtually nil in the erect position. The systolic pressure in the pulmonary artery is 20 to 25 mm. Hg, the diastolic pressure is 5 to 7 mm. and the average mean pulmonary arterial pressure as it leaves the heart is 15 to 18 mm. Hg. A column of blood 20 to 25 cm. in height exerts an equal (and opposite) pressure by its hydrostatic effect. The apex of the lung is 15 to 30 cm. cephalad to the pulmonary artery and therefore the pulmonary arterial pressure in the apex of the lung, with the patient seated or standing, is rarely over 10 mm. and in tall long-chested individuals it should be zero. The osmotic tension of the blood proteins is 25 mm. Hg and that of the tissue proteins is 10. There exists, therefore, an osmotic force of 15 mm. Hg which tends to keep fluids within the blood vessels and the systolic pressure must exceed this to produce an effective intra-arterial pressure which will force fluids (with oxygen, nutrients, antibodies, etcetera) into the tissues. Because of these facts Dock draws the following conclusions: (1) Little or no blood flows through the upper one-third of the lungs during two-thirds of the day. (2) No tissue fluid or lymph is formed there while the patient is in the erect position. (3) Little or no carbon dioxide or oxygen exchange can take place nor can antibodies be formed nor can removal of bacteria or dilution of their products take place. Dock suggests that tubercle bacilli are inhaled into all parts of the lungs but host resistance is usually great enough to destroy them in those sections of the lungs having adequate blood supply. In the apices of the upper lobes, however, for the reasons given above, the forces of host resistance are reduced in efficiency.

Why then does lower lobe tuberculosis develop? Dock reasons that, as most people can destroy tubercle bacilli which find their way to the lower lobes, the

development of active disease in these areas must be a manifestation of an inherently lowered resistance. Such patients, he feels, should not be benefited by bed-rest, which, he believes, may exert its desirable effect in upper lobe tuberculosis largely by virtue of the increased blood pressure produced in the involved area when the patient is recumbent.

Each one of the present series of 48 patients was studied from the standpoint of whether an unusually low resistance to tuberculosis was evident. It must be remembered that in no case was the lesion located above the level of the main pulmonary arterial shadow on the erect postero-anterior roentgenogram. It is understood that no predictable course can be expected in the individual case of tuberculosis but it is believed that in a group of this size an approach can be made to the problem. The following criteria were set up for evidence of lowered resistance: (*a*) steady spreading disease with little fibrosis and healing; and (*b*) rapid clinical downhill course with febrile episodes and progressive caseation.

Of the 48 cases analysis reveals that only 5 showed evidence of decreased resistance when these criteria were applied to each one individually.

The subsequent course of the group is in agreement with this evaluation. Of 48 patients (of whom 46 had moderately or far advanced disease at the time of admission to this hospital) followed for an average of three years, only five (10 per cent) are dead and 40 per cent have arrested lesions. Most of the patients with arrested lesions reached this clinical status without major collapse measures. Bed-rest, phrenic crush and pneumoperitoneum accounted for all but 4 of the arrested lesions.

The results observed in this group of patients do not appear to support the validity of the idea that patients with lower lobe disease have inherently lowered resistance to tuberculosis and hence develop the disease in this atypical location.

In the other series of cases studied (2, 3) the same conclusion was reached, *i.e.*, that the clinical course and prognosis in lower lobe disease parallels that of tuberculosis in the more usual distribution. It seems probable that poor results with therapy, which give rise to the impression that disease in this location is refractory to treatment, are due to mechanical factors rather than immunological ones. The high percentage of bronchial disease found in this series plus the related bad results with pneumothorax play a large part. In addition there exists the reluctance of the surgeon to perform thoracoplasty in cases where the upper one-half of the lung field is normal. There seems no evidence to substantiate Dock's theory that this localization is in itself evidence of lowered resistance or immunity. This is not, of course, an effort to support or disprove Dock's basic analysis of the vasodynamics of the lung and its relationship to upper lobe localization.

SUMMARY

1. Lower lobe tuberculosis is a fairly frequent problem in the diagnosis and treatment of pulmonary disease.

2. It is often misdiagnosed when first seen clinically and radiologically. Some of the reasons for this are discussed. Repeated sputum studies for tubercle bacilli, including cultures and gastric lavage, as well as repeated roentgenograms

should be obtained in the presence of lower lobe inflammatory lesions which fail to clear rapidly and completely. Lateral and oblique roentgenograms may be of value in clarifying the diagnosis. The possibility of tuberculosis cannot be dismissed as long as roentgenographic findings persist.

3. Most patients with lower lobe tuberculosis have bronchoscopic or radiologic evidence of bronchial disease. This must be considered in the diagnostic and therapeutic management of these cases.

4. Artificial pneumothorax almost always gives unsatisfactory results in this type of lesion.

5. No ideal type of therapy is demonstrated by study of this series. It seems probable that a short period of bed-rest followed by phrenic crush and pneumoperitoneum will offer the best results. Even this, however, is frequently unsuccessful. In addition, little is known of the ultimate fate of the patients who become arrested under this regimen.

6. The status of such measures as resection and cavernostomy plus streptomycin, either as primary treatment or in refractory cases, has as yet to be sufficiently explored.

7. Patients with lower lobe tuberculosis apparently do not have decreased resistance to this disease. The prognosis is approximately the same as that of patients with disease of similar extent in the upper lung fields. Difficulties in treatment would appear to be mechanical rather than immunological.

SUMARIO

Tuberculosis Pulmonar del Lóbulo Inferior

1. La tuberculosis del lóbulo inferior del pulmón constituye un problema bastante frecuente en el diagnóstico y tratamiento de las neumopatías.

2. Al ser observada por primera vez clínica y radiológicamente, es a menudo diagnosticada erróneamente, y aquí se discuten algunas de las causas de ello. En presencia de lesiones inflamatorias del lóbulo inferior que no desaparecen rápida y completamente, hay que hacer repetidos estudios del esputo, incluso cultivos y lavado gástrico, en busca de bacilos tuberculosos, así como radiografías repetidas. En el esclarecimiento del diagnóstico las roentgenografías laterales y oblicuas pueden resultar útiles. En tanto que persistan los hallazgos radiográficos no cabe descartar la posibilidad de tuberculosis.

3. La mayor parte de los enfermos con tuberculosis del lóbulo inferior muestran signos broncoscópicos o radiológicos de afección bronquial, lo cual hay que considerar en la atención diagnóstica y terapéutica de estos casos.

4. En esta forma de lesión el neumotórax terapéutico casi siempre da resultados poco satisfactorios.

5. El estudio de esta serie no ha revelado ninguna terapéutica ideal. Parece probable que un breve período de descanso en cama seguido de la trituración del frénico y el neumoperitoneo es lo que ofrece más promesa, y aun esto frecuentemente no da resultado. Además, poco se sabe del destino definitivo de los enfermos que se estacionan con este régimen.

6. Está aun por explorar a fondo el estado de medidas tales como la resección

y la cavernostomía, unidas a la estreptomicina, ya como tratamiento primario o en los casos refractarios.

7. Los enfermos con tuberculosis del lóbulo inferior aparentemente no muestran menor resistencia a la enfermedad. El pronóstico es aproximadamente idéntico que en los que tienen enfermedad de proporciones semejantes en los campos superiores del pulmón. Las dificultades terapéuticas parecen ser mecánicas más bien que inmunológicas.

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POOR RESULTS WITH ARTIFICIAL PNEUMOTHORAX IN LOWER LOBE TUBERCULOSIS[1, 2]

EMIL ROTHSTEIN

In a recent study of lower lobe tuberculosis (1), two related observations were made: The incidence of bronchial disease was unusually high and the results with artificial pneumothorax were very poor. In this paper these results are considered in detail.

CLINICAL MATERIAL

Seventeen patients were studied. One, however, had bilateral pneumothorax for bilateral lower lobe cavitation so an analysis of 18 pneumothoraces will be made. All of the patients were males. The average age was 28 years. Four were Negroes and the remainder were white. A positive bacteriologic diagnosis of tuberculosis was made in each case. Ten of the lesions were in the right lower lobe and eight in the left lower lobe. The average time between the first appearance of the lesion on the roentgenograms and the induction of the pneumothorax was eight months.

Description of the lesions: The lesion was moderately advanced in each instance at the time of induction of the pneumothorax. In all but 2 cases definite cavitation was visible and in the 2 exceptions the lesion was pneumonic in character with cavitation presumed but not demonstrated radiologically. In the cases showing excavation, the cavity was in the apex of the lower lobe (appearing to be hilar on the postero-anterior projection) in 7 and lower in the lung field in 9. The upper lung fields were essentially normal in all cases or presented a recent minimal extension of the lower lobe tuberculosis which was of little immediate significance.

Bronchial involvement: Direct or indirect evidences of bronchial involvement were present in all but one case. The following findings were considered to indicate tuberculous disease of the draining bronchus or bronchi: (*1*) bronchoscopic findings of stenosis or inflammation in the involved lobe; (*2*) partial atelectasis of the involved lobe either prior to or immediately after the induction of the pneumothorax; or (*3*) cavity changes consisting of fluid levels or fairly rapid changes in the size and the shape of cavities. Most of these last mentioned findings occurred in typical tension cavities which were round or oval with clear inner borders and relatively normal peri-cavitary lung fields. Twelve of the cavities presented fluid levels while sudden changes in size were recorded in 13. Atelectasis of a segment of the lower lobe was present in 5 cases before pneumothorax and in 5 immediately after its induction. Bronchoscopic changes were noted in 6 of the 9 cases in which bronchoscopy was performed. Thus it can be seen that many patients presented two or three of these manifestations.

[1] From the U. S. Veterans Administration Hospital, Tuberculosis Division, Wood' Wisconsin.

[2] Published with permission of the Chief Medical Director, Department of Medicine and Surgery, Veterans Administration, who assumes no responsibility for the opinions expressed or conclusions drawn by the author.

RESULTS WITH ARTIFICIAL PNEUMOTHORAX

The goal to be achieved with artificial pneumothorax is arrest of the tuberculous process, leaving a lung which re-expands and has a fairly good residual respiratory function. Serious pleural complications must be absent. The writer believes, with most other phthisiotherapists, that pneumothorax should be a reversible procedure which conserves much of the function of the involved lung. It is thought that a fibrothorax with a nonfunctioning lung, or an unexpandable lung with permanent pneumothorax or persistent effusion, must be considered a poor result even if the disease in the underlying lung is apparently inactive. It is on the basis of this evaluation that the following analysis was made.

In none of the 18 cases was a satisfactory result obtained (table 1). In 6 cases inoperable adhesions led to the discontinuation of the pneumothorax after an average period of six months. In 4 cases pneumothorax was stopped after four

TABLE 1

Reasons for poor results in pneumothorax cases of lower lobe tuberculosis

Inoperable adhesions	6
Massive recurrent effusions	5
Persistent cavity without adhesions	4
Voluntary discontinuation	1
Unexpandable lung	1
Progressive atelectasis	1
Total	18

to six weeks; 2 pneumothoraces were continued in other hospitals for twelve and twenty-one months, respectively. One patient has had lobectomy and 2 are scheduled for thoracoplasty but all 6 with inoperable adhesions still have active tuberculosis.

In 5 cases persistent massive pleural effusions led to the cessation of pneumothorax after an average period of eleven months of collapse. Fluid appeared on an average of five months after the onset of collapse therapy. In 2 of these patients acid-fast bacilli were present in the fluid but no purulent empyema developed. One patient has had thoracoplasty for an unexpanded lung, a second is undergoing thoracoplasty for an ipsolateral upper lobe cavity which developed subsequently, a third still has active disease, and the other two have arrested lesions. Both of the latter have badly crippled shrunken lungs due to inadequate expansion and fibrothorax. Unfortunately, the last statement is supported only by clinical observations as bronchospirometric readings are not available in either case.

In 4 cases open cavitation persisted despite the absence of evident adhesions. Pneumothorax was discontinued after an average period of fourteen months in this group. In general, the treatment was continued for such a long period because of cavities which would be lost to view temporarily, only to reappear six or eight months later. One of these lesions became arrested following phrenic crush and pneumoperitoneum. In a second case cavity closure apparently occurred following open cavernostomy and streptomycin. A third patient had thoraco-

plasty for further ipsolateral extension while the fourth still has active disease. In one of these cases a tension cavity increased considerably in size while pneumothorax was being administered.

Three miscellaneous causes of failure were as follows. In one case unexpandable lung accompanied by persistent effusion necessitated thoracoplasty. This patient's disease then became arrested. In a second case progressive atelectasis developed along with a pleural effusion which contained tubercle bacilli. The pneumothorax was discontinued and a phrenic crush was performed with subsequent arrest of the disease. The third patient voluntarily discontinued the treatment three months after apparent cavity closure. The cavity reopened one year later and the disease spread to both lungs.

The present status of the series is as follows: In 5 patients the disease is arrested, in 2 with pneumothorax alone. In both of these the result is considered unsatisfactory because of shrunken lung plus fibrothorax. The disease has become arrested in an additional 3 patients after thoracoplasty, phrenic crush, and phrenic crush plus pneumoperitoneum, respectively. The remaining 13 patients in the series all have persistent active tuberculosis.

SUMMARY

Eighteen lower lobe tuberculous lesions were treated with artificial pneumothorax. All were in males and the lesions were all moderately advanced. All but 2 were frankly cavitary. Only 2 became arrested with artificial pneumothorax therapy alone and in these instances the patients were left with shrunken lungs and thickened pleura. Three of the remaining lesions became arrested with other methods of treatment and the 10 others are still active.

It is believed that the poor results observed are in part due to the high incidence of bronchial disease as shown by bronchoscopy or by secondary pulmonary changes.

SUMARIO

Malos Resultados del Neumotórax Terapéutico en la Tuberculosis del Lóbulo Inferior

Dieciocho lesiones tuberculosas del lóbulo inferior fueron tratadas con el neumotórax artificial. Todas eran en varones y todas eran moderadamente avanzadas. Todas, menos dos, eran netamente cavitarias. Sólo dos, o sea 11.1 por ciento, se estacionaron bajo la acción exclusiva del neumotórax terapéutico, y en esos casos los enfermos quedaron con pulmones contraídos y pleuras espesadas. Tres de las lesiones restantes se estacionaron con otras técnicas terapéuticas, y las otras se hallan todavía activas.

Parece que los malos resultados observados se deben en parte a la alta incidencia de afección bronquial (95 por ciento) según revelaran la broncoscopia o las alteraciones pulmonares secundarias.

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PROGNOSIS OF INSPISSATED CAVITIES[1,2]

ROBERT S. STUDY[3] AND PHILIP MORGENSTERN[4]

INTRODUCTION

What is the prognosis of the inspissated cavity in tuberculosis? Several writers during the past ten years (9, 10, 12, 16, 17) have presented pathological and physiological evidence that inspissation is not an uncommon method of cavity healing. In spite of this fact, the idea has persisted among most chest physicians that an inspissated cavity is a dangerous, unstable lesion which may discharge its contents into the bronchus at any time. In the English literature only Shamaskin (14) has ventured the opinion that an inspissated cavity is a retrogressing or healed lesion and should be treated conservatively. He based his conclusions on a study of six cases.

Since the appearance of Shamaskin's article in 1941 (14), the question of prognosis in an inspissated cavity with negative sputum has assumed increased importance. This is due largely to advances in thoracic surgery, particularly in pulmonary resection. Many thoracic surgeons now regard the inspissated cavity as a definite indication for lobectomy. Is this attitude justified? The present study was undertaken to clarify the prognosis of the inspissated cavity and to evaluate the indication for lobectomy in such cases.

CASE REPORTS

A survey of approximately 1,000 patients now in the hospital or recently discharged and being followed in the outpatient department revealed 24 cases in which inspissated cavities were present. Under this heading were included only those cases where serial roentgenograms revealed a definite open cavity which became filled with secretions, was transformed into a dense opacity, and then began to decrease in size as the process progressed. All but 2 of the cases showed acid-fast bacilli in the sputum at the time they came under our observation.

In table 1 may be seen the pertinent data concerning the course of inspissation of the cavities in 24 patients who have been observed for periods ranging from six months to seven and one-half years. In the following paragraphs the clinical course of the first 6 patients shown in the table are described in detail. Serial chest roentgenograms illustrate the typical changes occurring in cavities during the process of "inspissation."

Case 1 (A. D. H.): The onset of this patient's tuberculosis was in September 1942. The admission film at Oteen on November 19, 1942 (figure 1) revealed disease in the basal

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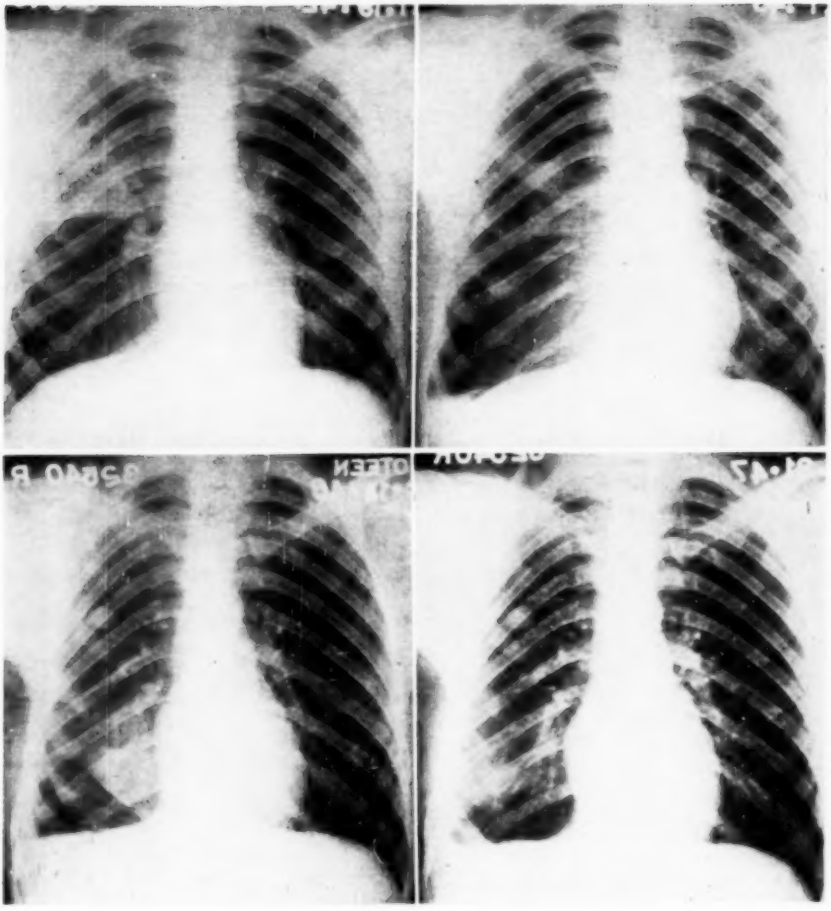
TABLE 1

NUMBER	NAME	ONSET	COLLAPSE THERAPY	CAVITY FIRST SEEN	CAVITY "INSPISSATED"	BACTERIOLOGY		
						Date of last sputum positive for tubercle bacilli	Subsequent sputum examination	
							Negative microscopics	Negative cultures
1.	A. D. H.	Sept. 1942	Pnx.† 12/ 2/42 8/14/46	11-19-42	1- 1-43	1-18-43	44	0
2.	H. I.	Dec. 1927	Phr.* 1932 Pnx. 1932-33	1-20-40	11-28-40	5-28-40	38	3
3.	J. T. U.	Mar. 1943	None	10- 7-43	1-26-46	9-27-44	26	4
4.	W. E. D.	Feb. 1943	Pnx. 11-19-43 3-25-47 Phr. 4- 4-47	9-18-43	7-21-44	2- 5-44	32	4
5.	T. A.	1941	Phr. 6-22-46 Pnm.‡ 8-13-46	4-12-44	8- 8-46	5-27-45	11	7
6.	W. W.	June 1946	Phr. 9-11-46	7-19-46	12-12-46	None	13	5
7.	T. F.	May 1942	Phr. 5-5-44, 2-8-45, 5-15-45 Pnx. 10-2-45	9- 6-43	12-14-45	5-17-45	10	8
8.	C. L.	Apr. 1944	Pnx. 7-8-44 2-5-46	4-11-44	3-14-45	7-12-44	22	6
9.	J. E.	Mar. 1943	None	5-14-45	10-23-45	5-10-45	5	4
10.	L. S. A.	Apr. 1943	Phr. 6-2-44 and 7-4-45 Pnx. 2-8-45 6-20-45 Pnm. 8-9-44 3-10-45 and 8-6-46 to date	6-28-44	1-10-47	3-20-46	5	4
11.	E. A. S.	Nov. 1945	Phr. 3-12-46 Pnm. 5-1-46 to date	2-11-46	lower cavity inspissated 5-24-46, upper on 8-14-46	5-24-46	6	3
12.	P. F.	Apr. 1946	Phr. 7-22-46 Pnm. 8-13-46; 9-20-46	6-22-46	9-20-46	7-12-46	10	3
13.	J. B.	July 1946	Phr. 9-2-46 and 7-22-47	8-12-46	3- 3-47	None Positive	6	1
14.	D. H.	Jan. 1946	Pnx. 9-24-46 to date Pneumonolysis 5-9-47	8- 7-46 2 cavities	Lower cavity inspissated first; upper inspissated 5-14-47	7-10-46	12	2

TABLE 1—*Continued*

NUMBER	NAME	ONSET	COLLAPSE THERAPY	CAVITY FIRST SEEN	CAVITY "INSPISSATED"	BACTERIOLOGY		
						Date of last sputum positive for tubercle bacilli	Subsequent sputum examinations	
							Negative microscopics	negative cultures
15.	J. A. S.	Mar. 1946	Pnx. 8-6-46 to date	6-17-46	8-16-46	8-20-46	14	6
16.	W. G.	Oct. 1946	Phr. 12-5-46 Pnm. 1-8-47 to date	11-21-46	2- 7-47	11-26-46	12	7
17.	R. H.	Nov. 1945	Pnx. 1-8-47 1-31-47 Pnm. 2-4-47 5-26-47 Phr. 2-14-47 Pregnancy delivered 9-9-47	12-27-46	2- 6-47	1-10-47	16	2
18.	C. P.	May 1943	Pnx. 2-21-44 4-4-44 Phr. 10-26-45 Streptomycin for endobronchial tuberculosis	1-29-44	1-30-46	2-18-47	6	3
19.	A. G. E.	Aug. 1946	Phr. 11-26-46 Pnm. 12-4-46 to date	10-23-46	1-14-47	3-22-47	11	5
20.	J. A. G.	Oct. 1946	Phr. 2-11-47 5-5-47 Pnm. 12-10-46	11-19-46 Two cavities	Upper cavity inspissated 4-2-47 and lower inspissated 7-16-47	4-7-47	4	0
21.	G. B.	Oct. 1946	None	3-14-47	7- 9-47	5-14-47	21	1
22.	A. S.	Nov. 1946	Phr. 5-13-47 Pnm. 6-30-47 to date	12-23-46	6-23-47	5- 1-47	9	0
23.	R. C.	Jan. 1947	Pnx. 6-12-47 to discharge Pneumonolysis 8-6-47	5-20-47	6-23-47	5-27-47	1	0
24.	G. D.	Feb. 1947	Pnx. 5-6-47 to date Pneumonolysis 7-8-47	4- 2-47	6-10-47	4-23-47	10	0

* Phr. = phreniclasia.
† Pnx. = Pneumothorax.
‡ Pnm. = pneumoperitoneum.



FIGS. 1-4

FIG. 1. (upper left) Case 1. (A. D. H.). Admission film of November 19, 1942, showing disease in basal portion of right upper lobe with a 2 cm. cavity in second anterior interspace.

FIG. 2. (upper right) Case 1. Chest film, January 1, 1943, one month after institution of pneumothorax. The cavity is seen replaced by an irregular nodular density.

FIG. 3. (lower left) Case 1. Film of August 14, 1946. The nodular density representing a presumably inspissated cavity has become considerably smaller since 1943.

FIG. 4. (lower right) Case 1. Film of July 21, 1947. The lung is now completely re-expanded and the nodular density in the right infraclavicular region shows beginning calcium deposition.

portion of the right upper lobe with a 2 cm. cavity in the second anterior interspace. The sputum was positive for acid-fast bacilli. A right pneumothorax was instituted

December 2, 1942, and the sputum became negative for tubercle bacilli in February 1943. The film on January 1, 1943 (figure 2) showed that the cavity had been replaced by a nodular density interpreted as an inspissated cavity. On serial films through 1947 (figures 3, 4) it was noted that the "inspissated" cavity had become progressively smaller with deposition of some calcium deposits in the outer portions of the density. The pneumothorax was discontinued August 14, 1946, and the lung re-expanded uneventfully.

Comment: This patient's sputum has been negative for tubercle bacilli for almost five years and the "inspissated" cavity shows no signs of breaking down.

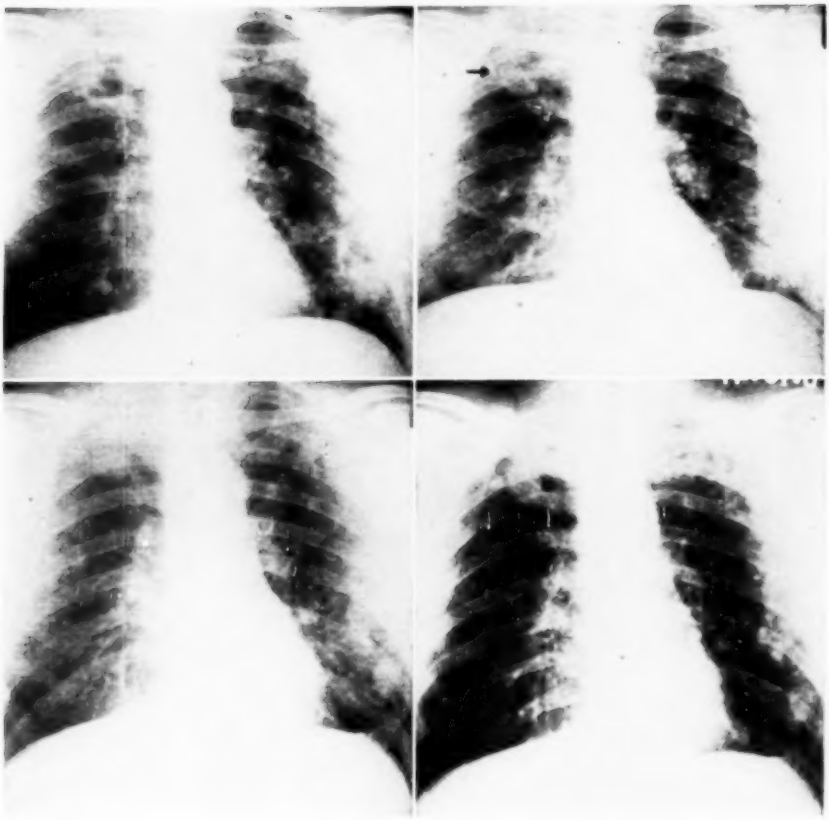
FIGS. 5–6

FIG. 5. (left) Case 2 (H. I.). Film of May 23, 1940, showing the small cavity in the right infraclavicular region just prior to inspissation.

FIG. 6. (right) Case 2. Film of August 26, 1947. The inspissated cavity in the right infraclavicular region has remained unchanged over a period of seven years.

Case 2 (H. I.): This patient was found to have tuberculosis in 1927. During the next thirteen years he was admitted to several tuberculosis sanstoriums. He was admitted to Oteen, January 19, 1940, with the diagnosis of moderately advanced pulmonary tuberculosis. His sputum was positive for acid-fast bacilli and a small thick-walled cavity was seen behind the second anterior rib on the right on January 20, 1940. Previous therapy consisted of a left phreniclasia in 1932 and a left pneumothorax in 1932–1933. His last sputum positive for tubercle bacilli was on May 28, 1940. The cavity was last seen May 23, 1940 (figure 5) and it was interpreted as "inspissated" on November 28, 1940. He was discharged as an arrested case in September 1943. Serial roentgenograms from November 1940 through August 26, 1947 (figure 6) have shown no appreciable change in the appearance of the "inspissated" cavity. He has had two admissions to Oteen since 1943, one for chronic bronchitis, the other for an upper respiratory infection. All sputum studies have remained negative for tubercle bacilli.

Comment: This case of an "inspissated" cavity has been followed for seven years and shows no tendency to exacerbation of the disease.



FIGS. 7–10

FIG. 7. (upper left) Case 3 (J. T. U.). Film of July 11, 1944, showing the large cavity in the right upper lobe with a basal fluid level.

FIG. 8. (upper right) Case 3. Film of December 6, 1944. The cavity in the right upper lobe is smaller, and the fluid level (indicated by arrow) is higher.

FIG. 9. (lower left) Case 3. Film of January 26, 1946. The cavity in the right upper lobe has been completely replaced by a uniform oval density which presumably represents an inspissated cavity.

FIG. 10. (lower right) Case 3. Film of June 19, 1947. The inspissated cavity is smaller and more sharply delineated.

Case 3 (J. T.U.): The onset of this patient's tuberculosis was in March 1943. Admission film of October 7, 1943, at Oteen showed a thick-walled cavity 5 by 3.5 cm. in the right infraclavicular region. The sputum was positive for acid-fast bacilli. A roentgenogram of July 11, 1944 (figure 7) showed extension of the disease to the left lower lung field. A fluid level was seen within the cavity in the right upper lobe and by December 6, 1944 (figure 8) the cavity had become definitely smaller with a thicker wall and a higher fluid

level. The last sputum positive for tubercle bacilli was on September 27, 1944. A chest film of January 26, 1946 (figure 9) was believed to show complete "inspissation." Serial roentgenograms taken through 1946 and 1947, the last on June 19, 1947 (figure 10), showed progressive contraction of the "inspissated" cavity with the formation of a hard nodular focus. The patient was discharged from the hospital on June 25, 1947.

Comment: This is a case of an "inspissated" cavity followed for over three years. The resulting nodular density has become progressively smaller. His sputum became noninfectious sixteen months before complete "inspissation" was demonstrated by roentgenography. During a period of more than three years examination of this patient's sputum with 14 direct smears, 12 concentrates, three cultures and one guinea pig inoculation has revealed no tubercle bacilli.

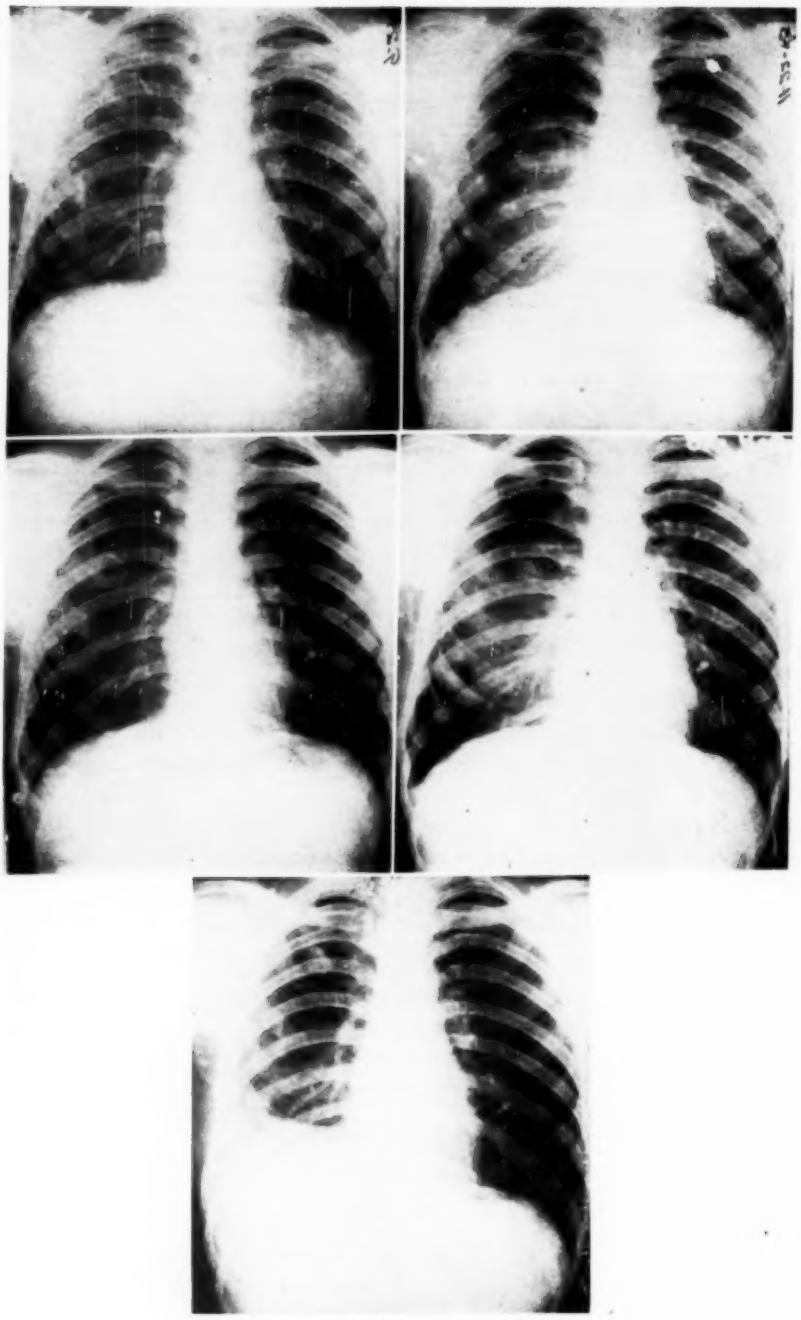
Case 4 (W. E. D.): The onset of this 24-year-old patient's tuberculosis was in February 1943. On September 29, 1943 (figure 11), a 3 cm. cavity with a basal fluid level was demonstrated in the right infraclavicular region by roentgenography. The sputum was positive for acid-fast bacilli and a right pneumothorax was instituted in November 1943 (figure 12). The patient was admitted to Oteen on January 3, 1944. By February 1, 1944, the cavity had diminished in size and was one-third filled with fluid (figure 13). His last sputum positive for tubercle bacilli was in February 1944, and by July 1, 1944, the cavity had been replaced by an oval density. In serial films taken on August 9, 1946 and August 22, 1947 (figures 14, 15), the stationary character of this nodular focus is demonstrated. This patient was discharged in September 1945, and the pneumothorax was discontinued in March 1947. Numerous sputum examinations since February 1944 have all been negative for tubercle bacilli.

Comment: This patient's sputum has been negative for tubercle bacilli for over three and one-half years and complete "inspissation" has been observed for approximately three years.

Case 5 (T. A.): The onset of this patient's tuberculosis was in 1941. He was admitted to Oteen April 11, 1944. On roentgenography a thick-walled cavity with a diameter of 4 by 6 cm. was seen in the left upper lobe and there was fibrocaseous involvement in the upper one-third of the right lung. The left upper lobe cavity remained unchanged in size (figure 16) until March 2, 1945, when it became smaller and showed a definite fluid level (figure 17). The patient's last sputum positive for acid-fast bacilli was May 27, 1945. Planigrams on June 22, 1946 (figure 18) showed the cavity to be still present. By August 8, 1946, the cavity was believed to be completely "inspissated." Films taken throughout the rest of 1946 and during 1947 showed the "inspissated" cavity to have become smaller, and a planigram on July 19, 1947 (figure 19) verified the stable character of the lesion. Since May 27, 1945 examination of the sputum (eight concentrates, seven cultures) has failed to reveal tubercle bacilli.

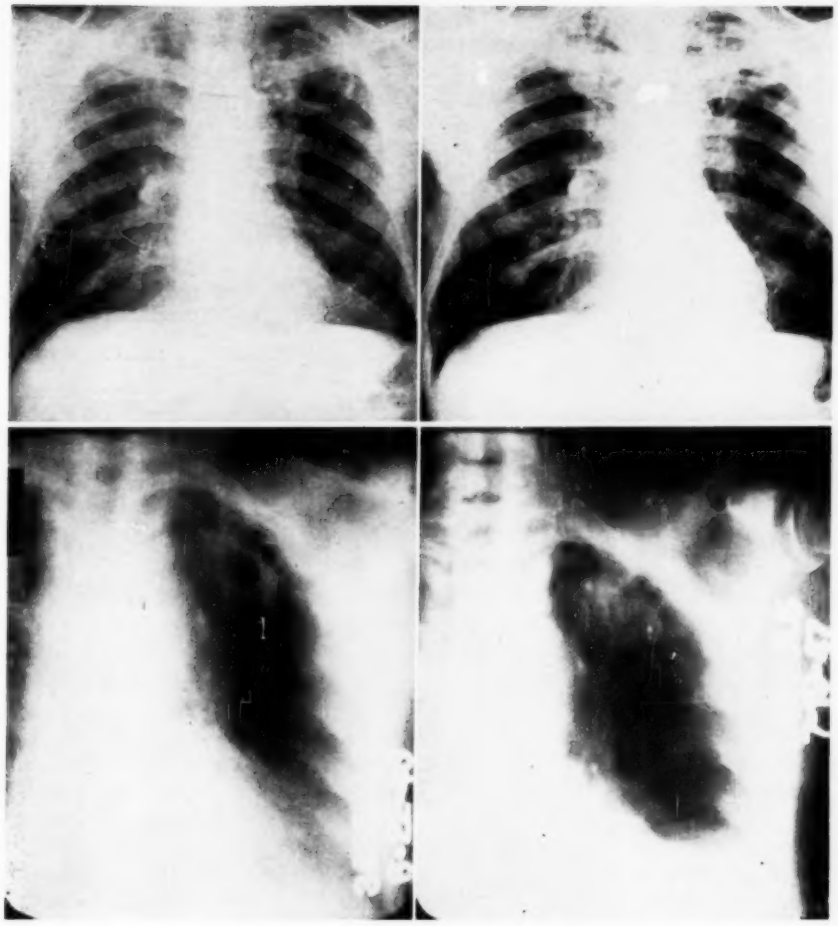
Comment: This patient's sputum has been negative for tubercle bacilli for two and one-half years and he is now on an ambulant status preparatory to being discharged.

Case 6 (W. W.): The onset of this patient's tuberculosis was in June 1946. At the time of his admission to Oteen on July 19, 1946, roentgenography revealed a small thick-walled cavity behind the left first anterior rib (figure 20). Numerous sputum studies failed to reveal acid-fast bacilli. The diagnosis of chronic pulmonary tuberculosis was based on



FIGS. 11–15

FIG. 11. (upper left) Case 4 (W. E. D.). Chest film of Sept. 29, 1943 shows a 3 cm. cavity with a basal fluid level in the right infraclavicular region.



FIGS. 16–19

FIG. 16. (upper left) Case 5. Chest film of September 28, 1944, showing 4 by 6 cm. cavity in left upper lobe. Tuberculous disease is present also in right upper lobe.

FIG. 17. (upper right) Case 5. Chest film of March 2, 1945. Cavity in left upper lobe is smaller and shows basal fluid level.

FIG. 18. (lower left) Case 5. Planigram of June 22, 1946 shows the contracted cavity in the left upper lobe. Sputum had already been negative for tubercle bacilli for one year at this time.

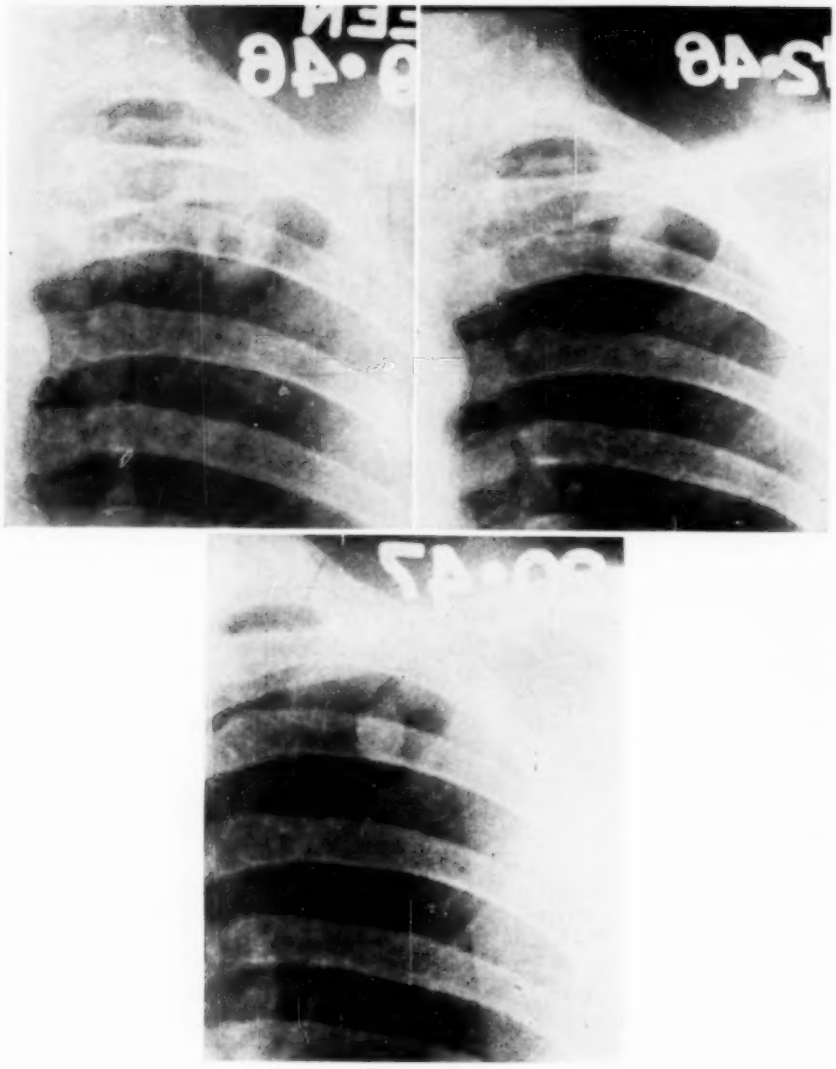
FIG. 19. (lower right) Case 5. Planigram of July 19, 1947, shows further progression of inspissation with disappearance of the central radiolucent area.

FIG. 12. (upper right) Case 4. Film of November 22, 1943. Pneumothorax has been instituted and cavity is still seen in compressed right upper lobe.

FIG. 13. (center left) Case 4. Film of Feburary 1, 1944. Cavity in right upper lobe is smaller and partly filled with secretions. Sputum negative for tubercle bacilli at this time.

FIG. 14. (center right) Case 4. Film of August 9, 1946. The nodular density in the right upper lobe represents inspissated cavity and has been present over two years.

FIG. 15. (bottom) Case 4. Film of August 22, 1947. Pneumothorax has been abandoned and inspissated cavity is still stable.



FIGS. 20–22

FIG. 20. (upper left) Case 6 (W. W.). Film of June 19, 1946, shows a small thick-walled cavity just below the left clavicle.

FIG. 21. (upper right) Case 6. Film of December 12, 1946, shows the cavity to have been replaced by a solid nodular density.

FIG. 22. (bottom) Case 6. Film of August 20, 1947. The inspissated cavity is slightly smaller and more sharply delineated.

chest roentgenograms showing a lesion typical of tuberculous cavitation, the history of recent blood spitting, daily temperature elevations, a chronic cough, and weight loss. On July 19, 1946, the tuberculin reaction was positive in the first strength using PPD. By December 12, 1946, the cavity was believed to have become completely "inspissated" (figure 21). Serial roentgenograms through August 1947 showed the lesion to have become progressively smaller (figure 22).

Comment: It is believed that the original "negative" sputum in this case can be explained by complete closure of the draining bronchus prior to the patient's hospitalization. This mechanism will be discussed later in the article.

DISCUSSION

The definition of an inspissated cavity should be thoroughly understood. It is one in which the draining bronchus has become firmly occluded, where the cavity is partially filled with secretions, and its contents have gradually thickened by the absorption of air and fluid. The finding of a horizontal fluid level within a cavity on a single chest roentgenogram is not adequate to warrant a diagnosis of permanent bronchial occlusion. On the contrary, it may indicate merely a temporary bronchial occlusion by a plug of mucus or debris which can be readily expelled. This is the so-called check-valve cavity. Only through serial films can the latter be differentiated from a cavity with a completely blocked bronchus followed by gradual absorption of air and progressive inspissation and shrinkage.

Likewise, an inspissated cavity should be differentiated from a caseous focus which has never ulcerated into a bronchus. The caseous parenchymal focus with ultimate excavation in its center is the ordinary method of cavity formation in reinfection type tuberculosis. In order to assume that a round nodular density seen on roentgenography is an inspissated cavity, there must be prior roentgenographic evidence of an open cavity in the same location.

In the past ten years a small number of articles have dealt with the mechanism of closure of tuberculous cavities. The actual anatomic evidence presented has been limited to some 39 cases (16, 17). Of these, inspissation was present in 22, being the most frequent form of healing observed in autopsy material. This seems like an extremely small number of cases when it is considered that literally hundreds of cavities have been observed in the course of collapse therapy in any large tuberculosis sanitorium. The discrepancy may be explained in two ways: 1. Those patients who collapse their cavities and "convert" their sputum are discharged and, in the main, are lost from sight and do not come to postmortem examination. 2. In those patients who die as a result of progressive pulmonary tuberculosis, what few healed cavities may be present are usually obscured by the mass of active disease. Nevertheless, several authors (Pagel (16), Auerbach and Green (12), Loesch (17)) have presented convincing anatomic evidence concerning the major mechanisms of cavity closure. These are: (*1*) closed type with inspissation or scar formation; (*2*) open type with nonspecific bronchiectatic epithelialization occurring in the cavitary wall and adjacent bronchus.

Prior to the work of these pathologists, Coryllos had adduced both theoretical

and experimental evidence to show that bronchial occlusion was of primary importance in cavity closure (1, 2, 3, 7, 8). He proved that complete closure of the bronchus through caseous bronchitis and resultant fibrosis (either in the course of bed-rest or secondary to the angulation of, and increase in pressure on, the bronchi resulting from collapse therapy) was followed by absorption of the air and shrinkage of the cavity. Coryllos clearly distinguished between this type and the temporarily blocked or check-valve cavity described by Eloesser (6) and Salkin, Cadden, and McIndoe (4). The latter will frequently balloon out and cause bronchogenic spread because of intermittent blockage by a caseous plug that subsequently may be dislodged.

In the article of Salkin *et al.* (4) which appeared in 1936, there was some confusion regarding the nature of blocked cavities. In a series of tuberculous patients who had just died they endeavored to delineate cavities and their draining bronchi. This was done with a radio-opaque material injected both into bronchi through the trachea and into cavities through the chest wall. Of 147 open cavities examined, 14 per cent did not communicate with a bronchus. Their conclusion was that blocking of a draining bronchus does not cause cavity healing.

Several fallacies should be pointed out in connection with their experiments. Certain changes occur in bronchi near or soon after the time of death. The patient has usually died in expiration (18) and lumina of the bronchi, therefore, will be narrowed. Caseous plugs, absence of respiratory movements and terminal fluid in the alveoli and bronchioles, combined with the narrowed bronchi of expiration, will cause additional bronchial stenosis. The above factors, together with the endobronchial disease known to be present near the opening of draining bronchi into cavities, may well completely occlude the bronchus. In a second article these authors admitted that blockage of bronchi often occurred due to blood, pus, secretions and entrapped air.

Although all cases of cavity closure may not be ascribed to a single mechanism according to the physiological principles enunciated by Coryllos, the draining bronchus must be of prime importance. Actually the term "inspissated cavity" is a relative one. It is highly improbable that all the caseous material is ever extruded from a cavity. With firm bronchial occlusion the retained mass is then subjected to the physiological effects of a continuing decrease in oxygen. Concomitantly with this decrease in oxygen, the metabolism of the tubercle bacillus drops. Experimentally, under such conditions the rate of growth of the bacilli may be markedly suppressed, although they may remain viable for long periods of time. Whether an inspissated cavity or a radiating scar is formed, some caseous material is always retained. Various workers have recovered viable tubercle bacilli from both types of lesions. Yet little hesitancy occurs in discharging a patient as an arrested case if a scar-type lesion has remained unchanged over a period of months. The entire concept of handling clinical tuberculosis would have to be changed if all patients were kept under hospital care until their lesions were pathologically healed. If a small mass of caseous material in the scar-type lesion is considered clinically inert, there seems to be no reason for considering a somewhat larger mass in a different light.

Whether inspissation or scar formation results may well depend upon the amount of material in the cavity at the time of bronchial occlusion, in addition to other factors such as the thickness of the cavitary wall (12). If the caseous contents have been recently extruded, the resultant mass will be smaller and eventually will contract to form a scar. If the cavity is filled at the time of bronchial closure, the resultant mass will become inspissated and remain as a round nodular density.

The idea that retention of secretions in a tuberculous cavity is harmful to a patient was based chiefly on the assumption that coexisting pyogenic organisms would cause superimposed infection. Coryllos (8), in the course of cavernostomy operations, investigated the contents of several cavities and found no pyogenic organisms on smear and culture. Even Pinner (13), who has been a leading proponent of the theory that toxemia results from retention of secretions within a cavity, has recently admitted that some cavities may follow the benign course outlined by Coryllos. The present findings in 24 cases confirm the deductions of Coryllos's physiological studies and the pathological investigations of Pagel (10), Auerbach (12) and Loesch (17).

In 20 of 24 cases the last sputum positive for tubercle bacilli was from one to sixteen months prior to the demonstration of "inspissation" by roentgenography. This is in accord with Coryllos's concept that bronchial closure precedes cavity closure. None of these patients demonstrated any clear-cut toxemic symptoms of retention.

In the past it has been the general concensus of opinion that these lesions are unsafe and eventually will empty their contents through the draining bronchus and cause a bronchogenic spread. In none of the cases of the present series has this catastrophe occurred although 8 have been followed for from two and one-half to seven and one-half years and 16 have been followed from six months to two years. Serial roentgenograms show these caseous areas to be consistently decreasing in size since "inspissation." There is good reason to believe that they will go on to calcification and permanent healing. Furthermore, in the past eighteen months at Oteen Hospital, where approximately 3,000 cases of pulmonary tuberculosis have been seen, not a single case has been observed in which a definite "inspissated" cavity has broken down. This would indicate that the latter phenomenon, although it may occur, is certainly very rare.

It should be clear that the writers are not questioning the accepted indications for pulmonary resection in certain well-defined tuberculous lesions. This procedure is generally considered to be justified in: (*1*) tuberculous bronchiectasis; (*2*) following thoracoplasty failure with a residual cavity; (*3*) basal tuberculosis which fails to respond to collapse measures; (*4*) tuberculoma. Actually the diagnosis of a tuberculoma is extremely difficult, and many round nodular lesions with an unknown diagnosis are proved to be tuberculous only following removal. Nor do the writers question the indication for exploratory thoracotomy and resection in cases of large nodular lesions of undetermined etiology (5, 11). All of the present cases involved "inspissated" tuberculous cavities which it is believed represent regressing lesions.

If, then, the inspissated cavity is accepted as being a relatively benign lesion, it ceases to be an indication for lobectomy. Examination of the tuberculous cavity at autopsy reveals that such cavities are almost never isolated lesions and caseous foci of varying size are generally scattered throughout the other lobes some of them too small to be visualized on a roentgenogram (19). It is obviously impossible to excise all the foci that may be present in a tuberculous lung. Thus it seems illogical to attempt a major surgical procedure to eradicate what is in the vast majority of cases a benign lesion, an inspissated cavity.

SUMMARY

1. The controversial subject of the fate of inspissated cavities has been discussed from the standpoint of diagnosis, pathogenesis and prognosis.

2. Twenty-four cases are presented in which presumably inspissated cavities have been followed for as long as seven and one-half years. Histories on six of these patients are given in detail, together with serial roentgenograms showing the course of inspissation.

3. It is concluded that a true inspissated cavity is essentially a benign lesion and has a favorable prognosis.

SUMARIO

Pronóstico de las Cavernas Espesadas

1. Discútese, desde el punto de vista del diagnóstico, patogenia y pronóstico, el debatido tema del destino de las cavernas espesadas.

2. Preséntanse 24 casos en los que cavernas presuntamente espesadas fueron observadas hasta siete años y medio. Se dan con todo detalle las historias clínicas de seis de esos enfermos, junto con radiografías seriadas que revelan la evolución del espesamiento.

3. Dedúcese que una verdadera caverna espesada es en el fondo una lesión benigna con un pronóstico favorable.

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THE EFFECT OF NONTUBERCULOUS PULMONARY INFLAMMATION ON PULMONARY TUBERCULOSIS[1,2]

OTTO S. BAUM AND LEWIS F. BAUM

INTRODUCTION

The following paper is an outgrowth of a study on the same subject (1), published in 1942 by Dr. J. Burns Amberson and one of the writers (O. S. B.), in which the effects of nontuberculous inflammation on pulmonary tuberculosis were observed. An apparent increase in the incidence of coexistent disease and a new therapeutic approach to the pneumonias has prompted an additional review of the subject.

The primary purpose of this paper is to determine: (*a*) the actual incidence of complicating nontuberculous inflammation; and (*b*) the effect of chemotherapy on the course of the underlying tuberculous process.

A brief resumé of the conclusions of the original report is in order. It was found that pneumonia in the tuberculous population was not as rare as formerly had been thought, that the necrotizing process[3] within a pneumonic area was the most important factor in activation of a tuberculous lesion located therein; and that the necrotizing process usually affected the tuberculous lesion adversely. Interstitial extension of the infecting organism from the alveoli, such as occurs in the pneumonias produced by type III *pneumococcus*, *hemolytic streptococcus*, *staphylococcus*, and *Friedländer's bacillus*, was also found to be one of the determining factors. The destructive change is also probably related to local toxins and the action of enzymes. Bronchorrhea and local hyperaemia may also play a role, particularly when the tuberculous lesion is located at a distance from the superinfecting process. Fibrocalcific lesions and lesions successfully controlled by collapse therapy were most resistant to breakdown.

Since 1942 there has been only one publication on this subject, that of Hogan (2) who studied 111 cases of pneumonia occurring in tuberculous individuals admitted over an eight year period to the Philadelphia General Hospital. It was his impression that the incidence of coexisting lesions was relatively low, and that pneumonia occurred primarily as a terminal event. In 15 per cent of his series he found evidence of activation of a tuberculous focus. This occurred whether the tuberculosis had previously been quiescent or active, whether or not it was situated in the same lobe with the pneumonia, and whether or not the latter was specifically treated. This study was made prior to the advent of penicillin

[1] From the Chest Service, Bellevue Hospital, New York, and Department of Medicine, College of Physicians and Surgeons, Columbia University, New York.

[2] Presented at the annual meeting of the New Jersey State Medical Society, April 1948.

[3] Much confusion exists in the literature concerning the terminology of the various types of pneumonia. The term "suppurative pneumonia" has frequently been employed to denote the presence of a necrotizing component of the disease process. In this paper the term "necrotizing pneumonia" is used to differentiate this process from purely intra-alveolar pneumonias and from interstitial (atypical, "virus") pneumonias.

therapy. It is of importance to note that the pneumonias in his study were primarily nonsuppurative. Moreover, his concern was mainly with the effect of tuberculosis on the complicating pneumonia in contrast to the approach of the present study.

CLINICAL MATERIAL

The material comprising the present study consists of all cases of proven coexisting tuberculosis and pneumonia, necrotizing and otherwise, discharged from the chest service of Bellevue Hospital between July 1941 and June 1947. All cases of tuberculous pneumonia, pneumonia secondary to tuberculous, or neoplastic endobronchial disease are excluded.

Evidence of activation of the tuberculous lesion was considered to be *definite* when there was: (*a*) post mortem evidence of recent activation; (*b*) progressive tuberculosis after pneumonia, and the tuberculosis had previously been stationary; (*c*) extension of previously active tuberculosis coincidentally with the pneumonia.

TABLE 1

Incidence of activation

PNEUMONIA			NECROTIZING PNEUMONIA		
Activation	Number	Per cent	Activation	Number	Per cent
Definite	16	13	Definite	21	55
Doubtful	9	8	Doubtful	4	11
No activation	91	78	None	11	29
Undetermined	1		Undetermined	2	5
Total	117	100	Total	38	100

Cases in which the pneumonia was accompanied or followed by the transient expectoration of tubercle bacilli or residual densities on the roentgenogram were classified as *doubtful*. The designation *undetermined* was used for those cases in which death occurred too quickly for proper evaluation or in which there was inadequate information regarding pre-existing tuberculosis.

A total of 155 cases, 38 of which were necrotizing pneumonias, has been reviewed. In table 1 the criteria of activation are applied separately to the pneumonias and necrotizing pneumonias. The high percentage (55 per cent) of activation in the necrotizing group is of interest.

The relationship between activation and the type of pre-existing tuberculous disease may be seen in table 2. The largest percentage of activation (11 per cent) is seen to occur in the "fibro-caseous" classification.

As was pointed out in the previous report, the bacteriology and location of the inflammatory lesion are of greatest importance in determining subsequent activation of the tuberculosis. In tables 3 and 4 may be seen the relationship of activation to these factors. It may be seen that organisms causing destruction of lung tissue are most likely to cause activation when the lesion produced

thereby is located in a tuberculous lobe. In contrast, the less destructive types of bacteria, especially when situated in a distant lobe, rarely cause activation.

TABLE 2

Relation between activation and type of disease (necrotizing pneumonias excluded)

ACTIVATION	TYPE OF TUBERCULOSIS					
	Fibro calcific		Fibro-caseous		Exudative	
	Number	Per cent	Number	Per cent	Number	Per cent
Definite	2	2	13	11	1	1
Doubtful	2	2	5	4	2	2
No activation	56	47	25	21	10	9
Undetermined			1	1		

TABLE 3

Relation between activation and bacteriologic findings

	Pneumococci				*Streptococci* OR *Staphylococci hemolyticus*	*K. pneumoniae*	MIXED AND UNDETERMINED
	I	II	III	Other *Pneumococci*			
Definite	1	3	1	9	4	4	16
Doubtful	0	0	1	6	1	0	5
No activation	5	9	4	21	2	1	59
Undetermined	0	0	0	0	1	0	2
Total	6	12	6	36	8	5	82

TABLE 4

Relation between activation and location

ACTIVATION	LOCATION OF TUBERCULOUS LESION AND NONTUBERCULOUS PNEUMONIA								
	Same lobe			Other lobes			Undetermined		
	P	N	T	P	N	T	P	N	T
Definite	13	14	27	1	7	8	2	0	2
Doubtful	3	4	7	5	0	5	1	0	1
No activation	18	0	18	73	11	84	0	0	0
Undetermined	1	2	3	0	0	0	0	0	0
Total			55			97			3

P = Pneumonia.
N = Necrotizing pneumonia.
T = Total.

Activation of the tuberculous process occurred in only 2 of 6 cases of *pneumococcus* type III pneumonia (table 3). This apparent contradiction to the findings in the previous paper of the very invasive nature of this organism is clarified

by referring to table 5 in which the relationship between activation, etiology of the acute pneumonia and its location are tabulated. It may be seen that 3 of the remaining 4 cases of *pneumococcus* type III pneumonia occurred in lobes other than those involved by tuberculosis. It is of interest to note that the fourth case of nonactivation occurred in a tuberculous lobe which was effectively collapsed by pneumothorax. In table 6 the relation of therapy to activation is tabulated. In this small number of cases chemotherapy appeared to have no effect on the percentage of activation.

TABLE 5

Relation between bacteriologic findings and location of the pneumonia to activation of tuberculosis

ACTIVATION	*Pneumococci*								*Streptococci* OR *Staphylococci hemolyticus*		*K. pneumoniae*		MIXED AND UNDETERMINED	
	I		II		III		Other *Pneumococci*							
	S	O	S	O	S	O	S	O	S	O	S	O	S	O
Definite	1	0	3	0	1	0	7	2	3	1	4	0	9	7
Doubtful	0	0	0	0	0	1	3	3	1	0	0	0	3	2
No activation	0	5	2	7	1	3	5	16	0	2	0	1	9	50
Undetermined	0	0	0	0	0	0	0	0	1	0	0	0	2	0
Total	6		12		6		36		8		5		82	

S = Same lobe. O = Other lobes.

TABLE 6

Relation of therapy to activation

	PNEUMONIA				NECROTIZING PNEUMONIA			
	Definite	Doubtful	No activation	Undetermined	Definite	Doubtful	No activation	Undetermined
Sulfonamides	5	5	46	0	5	2	2	1
Penicillin	9	3	12	0	7	0	1	1
Combined therapy	2	1	3	0	2	0	1	0
No specific therapy	0	0	30	1	7	2	7	0
Total	16	9	91	1	21	4	11	2

CASE REPORTS

Case 1: S. M., a 52-year-old white male, was admitted February 13, 1945 with one week's history of left chest pain, cough and rusty sputum. The patient was acutely ill, with signs of left lower lobe pneumonia. The total leucocyte count was 15,000 per cu. mm. The sputum contained type I *pneumococci* and was persistently negative for acid-fast bacilli. The patient was treated with sulfadiazine, with a dramatic clinical response but a slow resolution of pneumonia on the roentgenograms. There was no activation of an old left upper lobe infiltrate.

Case 2: J. K., a 61-year-old white male, was admitted to another hospital five days after onset of chills, fever, and cough. Left lower lobe pneumonia was diagnosed and treatment with sulfathiazole was started. Two days later, on January 27, 1944, he was transferred to the Psychiatric Division of Bellevue Hospital because of psychotic symptoms. On admission there were signs of a left lower lobe pneumonia and a leucocytosis of 11,000 cells per cu. mm. Results of bacteriologic studies of the sputum are unknown except for persistent absence of acid-fast bacilli. All symptoms subsided rapidly. The pneumonia resolved slowly. There was no activation of an old tuberculosis of the left and right upper lobes.

Case 3: W. A., a 21-year-old white male, had known tuberculosis since 1941 which had been treated by right pneumothorax since March 1942. He was admitted on July 15, 1943 with a four day history of fever, chills, cough, sputum, and chest pain. On admission he was acutely ill. The total leucocyte count was 11,000 per cu. mm. with 70 per cent polymorphonuclears. The sputum contained type III *pneumococci* and was persistently negative for acid-fast bacilli. A roentgenogram revealed pneumonia in the collapsed lung. The clinical symptoms subsided rapidly on sulfadiazine therapy and the roentgenographic findings reverted to the pre-pneumonia status. There was no activation of the tuberculous lesions.

Case 4: C. V., a 50-year-old white male, with known tuberculosis since 1938, treated by thoracoplasty in March 1942, was admitted on April 27, 1943 with a two day history of cough, sputum, fever, chills, and right chest pain. The temperature was 104° F. and the total leucocyte count was 11,000 per cu. mm. The sputum contained type XIX *pneumococci* and was persistently negative for acid-fast bacilli. Roentgenographic examination revealed a density in the collapsed right lung. The patient was treated with sulfadiazine with dramatic response although leukopenia developed on the third day and administration of the drug was stopped. There was progressive clearing of the density visible on the roentgenogram. The patient has been followed to date and no evidence of activation of his tuberculosis has appeared.

Case 5: P. L., a 46-year-old white male with known minimal right upper lobe tuberculosis since 1945 which had been treated by bed-rest in a sanatorium for one year, was admitted on April 7, 1947 with a two week history of upper respiratory infection and a one day history of right pleuritic pain and fever. He was moderately ill and had a leucocytosis of 18,000 cells per cu. mm. with 86 per cent polymorphonuclears. A chest roentgenogram revealed no extension of the minimal tuberculosis. The acute pneumonia was located in the apex of the right lower lobe. Culture of the sputum showed *streptococcus hemolyticus* and *streptococcus viridans, staphylococcus albus,* and *M. catarrhalis.* The patient was treated with penicillin with prompt clinical and roentgenological response. Unfortunately, however, there was a progressive increase in the formerly inactive tuberculous lesion. This case represents an instance of definite activation following an acute non-tuberculous pneumonia.

Case 6: P. P., a 45-year-old white male, had known tuberculosis of the right upper lobe since 1938 with subsequent spread to the left mid-lung. A cavity had been present in the right apex until 1940 when it closed. He was admitted November 4, 1942 with a short history of fever, cough and chest pain. There were signs of consolidation in the left lower lobe and type VIII *pneumococci* were found in the sputum. There was a prompt clinical response to sulfadiazine with complete clearing of the pneumonia and no acti-

vation of the tuberculosis. He was readmitted in October 1945 with a one week history of chills, fever, cough, sputum, and sudden left chest pain. On admission he was acutely ill, dyspneic, and cyanotic. The total leucocyte count was 20,000 per cu. mm. A roentgenogram of the chest showed a left lower lobe pneumonia with a left spontaneous pneumothorax. Sputum culture showed *streptococcus hemolyticus*, *streptococcus viridans*, and *E. coli*. The patient was treated with penicillin with complete resolution of the pneumonia and re-expansion of the left lung. The sputum was persistently negative for acid-fast bacilli. He was discharged in December 1945, but readmitted in February 1946 with a history of progressive cough, sputum and weight loss since discharge. The sputum contained acid-fast bacilli. A chest roentgenogram showed extensive left upper lobe disease with cavitation and subsequent marked spread. This case represents an instance of definite activation of tuberculosis following an acute nontuberculous pneumonia.

Case 7: D. R., a 68-year-old white male, was perfectly well until four days before admission in May 1941 when he began to have left chest pain and a productive cough. He was acutely ill with signs of left upper lobe lobar and scattered bronchopneumonia. The total leucocyte count was 22,000 per cu. mm. with 83 per cent polymorphonuclears. The sputum contained type III *pneumococci* and on 12 examinations was negative for acid-fast bacilli. The patient was treated with sulfadiazine and 175,000 units of serum with good clinical improvement, and he was discharged July 7, 1941. He was readmitted on September 5, 1941 because of cough beginning one month after discharge. The roentgenogram revealed an infiltration of the left upper lobe and throughout the right lung. The sputum was persistently positive for acid-fast bacilli. This case is considered to represent a definite activation following an acute nontuberculous pneumonia.

Case 8: D. G., a 41-year-old white male, was admitted on April 9, 1945 with a history of an alcoholic debauch on the previous New Year's Eve, followed by the aspiration of vomitus. In February he began to cough, producing one-half cup of mucopurulent, occasionally foul, sputum and complained of weakness and a 20 pound weight loss. Examination revealed a temperature of 100° F., foul gums, and rales over the right upper lobe. The first five sputum examinations were negative for acid-fast bacilli. Successively thereafter one was positive, nine were negative and two were positive. Subsequently the sputum examinations were intermittently "positive" from May until July. The total leucocyte count ranged between 7,000 and 14,000 cells per cu. mm. with 80 to 87 per cent polymorphonuclears. Cultures of the sputum revealed the usual mouth flora. On bedrest the patient gained weight and the lesion cleared rapidly. Bronchoscopy and bronchography were negative. It was felt that this was a necrotizing pneumonia with activation of a tuberculous focus.

Case 9: M. C., a 43-year-old white male alcoholic, was admitted November 21, 1941 with a one week history of cough, sputum, and fever. He was found to have a right upper lobe pneumonia and *K. pneumoniae*, type B, was cultured from sputum and blood. He was treated with sulfapyridine. He showed a slow clinical response with gradual excavation of upper lobe followed by a residual abscess. The patient refused permission for pulmonary resection.

He was followed for one and one-half years and no change was noted on the roentgenograms. Nevertheless, he had repeated acute respiratory episodes with several positive cultures for *K. Pneumoniae*, type B. Examination of the sputum was always negative for acid-fast bacilli.

He was readmitted December 6, 1943, having been lost from observation during the

preceding six months. On this admission he gave a history of cough, sputum and 36 pound weight loss in the preceding two months. Roentgenographic examination revealed extensive bilateral infiltration and the sputum was positive for acid-fast bacilli.

DISCUSSION

From the data presented it is evident that the incidence of the diagnosis of coexisting pulmonary diseases on the Chest Service of Bellevue Hospital has markedly increased. It is believed that this is due to an increased awareness of the possibility of such coexistence rather than an increase of pneumonia or tuberculosis, or of pneumonia occurring in the tuberculous. It is the impression of the writers that many cases of tuberculosis are overlooked when admitted to a general hospital with the diagnosis of pneumonia. One need only inquire into the past history of the average tuberculous individual to observe the great frequency of "pneumonia," with classical symptoms and findings, rapid subsidence of these symptoms with appropriate therapy, early discharge from the hospital, and subsequent readmission for active tuberculous disease. Obviously these cases cannot be included in such a study as the present one. It seems certain, however, that their number is great and that the actual incidence of coexisting pulmonary diseases is larger than any available statistics show. It is believed that a true picture can be obtained by attention to the following principles: (*1*) roentgenographic examination of all cases of pneumonia just before discharge from the hospital; (*2*) careful sputum studies in all suspicious cases; (*3*) close observation of all cases showing slow resolution of an acute pneumonia; and (*4*) particular attention to those cases where the course and bacteriological findings suggest the possibility of a necrotizing process.

The present data reinforce the concept presented previously that a tuberculous lesion is most likely to be activated by a pneumonia if the latter is necrotizing and is located in the same lobe. Although the greatest incidence of activation is in active fibro-caseous disease, the nature of the original tuberculous lesion is of relatively minor importance, as activation can occur in calcified primary lesions.

Despite the relatively small number in this series, the sulfonamide and penicillin treated cases show a rather high incidence of activation. Comparison with previous statistics shows that use of chemotherapy has not significantly changed the percentage of activation. One may speculate as to the probable reasons for this disappointing observation. Is it justified to assume that specific therapy of the pneumonia prolongs life and hence affords time for the progression of activated tuberculous disease? Or is it possible that in nonterminal cases the early invasive nature of the superinfecting organism initiates progression of the preexisting tuberculous lesion before chemotherapy has a chance to exert its bacteriostatic or bactericidal effect? Theoretically it seems likely that intensive specific therapy, if instituted early, would prevent the development of necrosis and thereby prevent activation of the underlying tuberculous disease. The disappointing results might thus be due to late initiation of therapy, a situation which might be remedied by the admission of patients early in the course of their pneumonia. Whether or not coincident administration of streptomycin

would prevent activation of the tuberculous process remains to be determined in further observations.

SUMMARY

1. A study of the effect of nontuberculous inflammation on pulmonary tuberculosis has been brought up to date. The increased incidence of coexisting disease is probably due to increasing awareness of the possibility.

2. The necrotizing component of a pneumonia is again shown to be of greatest significance in the activation of tuberculous infection. Location of the superinfection is again implicated.

3. Satisfactory collapse therapy militates against activation even when pneumonia is located in the collapsed lobe.

4. Adequate bacteriological identification of the superinfecting organism is essential to the proper management of the tuberculous disease and has a direct bearing on prognosis.

5. The present limited data indicate that antimicrobial therapy did not prevent activation of the tuberculous process. On theoretical grounds early intensive specific therapy might change these results.

SUMARIO

Efecto de la Neumonitis No Tuberculosa sobre la Tuberculosis Pulmonar

1. Se ha puesto al día un estudio del efecto de la inflamación no tuberculosa sobre la tuberculosis pulmonar. La mayor incidencia de esta coexistencia procede probablemente de la mayor atención prestada a su posibilidad.

2. Demuéstrase de nuevo que el factor necrotizante de una neumonía reviste importancia máxima en la activación de la infección tuberculosa. La localización de la superinfección es inculpada de nuevo.

3. La colapsoterapia satisfactoria milita contra la activación aun cuando la neumonía se localice en el lóbulo aplastado.

4. La adecuada identificación bacteriológica del microbio superinfectante resulta indispensable para la propia atención de la enfermedad tuberculosa y guarda relación directa con el pronóstico.

5. Los actuales y limitados datos indican que la terapéutica antimicrobiana no impidió la activación del proceso tuberculoso. Teóricamente, una intensa y temprana terapéutica específica podría alterar este resultado.

Acknowledgment

The authors wish to express their thanks to Dr. J. Burns Amberson for his invaluable assistance in the preparation of this paper.

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A SUPERNUMERARY RIB[1]

SYDNEY JACOBS

REPORT OF A CASE

B. T., a 43-year-old Negro male, was admitted to the Charity Hospital of Louisiana in May, 1946, because of bilateral far advanced pulmonary tuberculosis. On admission,

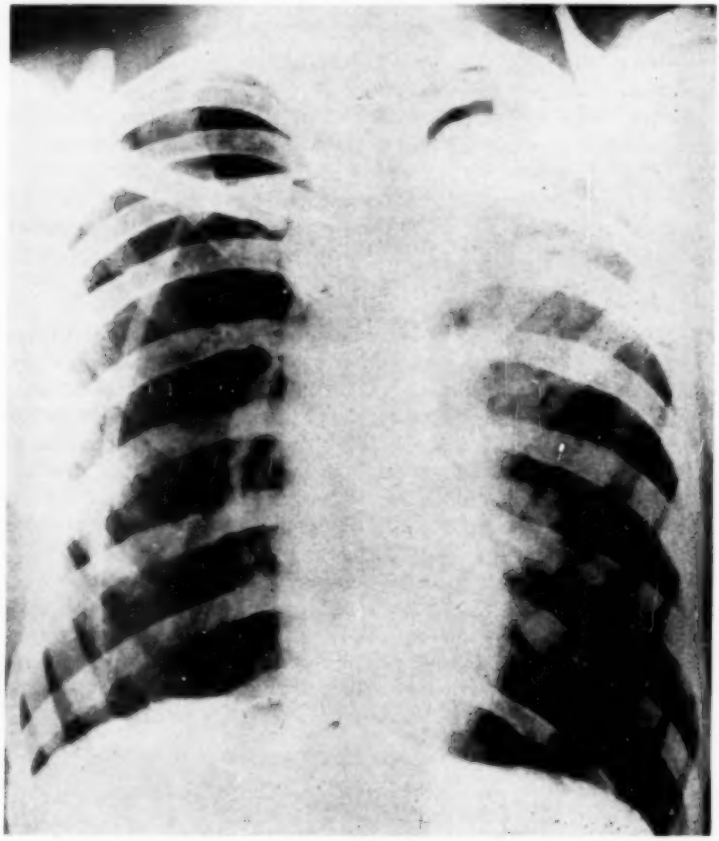

FIG. 1. Chest roentgenogram revealing supernumerary rib on the right.

there was roentgenographic evidence (figure 1) of a supernumerary rib. The patient died on June 27, 1946. At autopsy the most important findings were bilateral caseous pneu-

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monia with extensive cavitation, miliary tuberculosis of the spleen and kidneys, and syphilitic aortitis. No congenital anomalies other than the supernumerary rib were found.

When the right lung was removed, the supernumerary rib was seen originating from the third dorsal vertebra on its anterolateral surface, articulating independently of the normal rib arising from this vertebra. The rib coursed along the posterior thoracic wall downward and slightly laterally on the anterior surface of the normal ribs, external to the pleura. It terminated at the level of the eighth thoracic vertebra seven centimeters from the vertebral body. There were twelve pairs of thoracic ribs arising in normal manner.

About one per cent of persons have some variation from the normal pattern of twelve pairs of thoracic ribs. Extra ribs, in either the cervical or the lumbar region, may be single or paired. Occasionally one side of the thorax may have fewer than twelve ribs because of maldevelopment of a vertebra (1) or because of fusion of adjacent vertebral or costal segments. Such variations can easily be explained and are usually accompanied by other congenital anomalies.

The herein reported supernumerary rib cannot be similarly explained and was not found associated with other congenital anomalies. No description of a similar rib could be found in the literature.

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A TUBERCULOSIS CASE-FINDING PROGRAM IN ERIE COUNTY, NEW YORK

VINCENT H. HANDY[1] AND WILLIAM D. CRAGE[2]

INTRODUCTION

For many years Erie County, including the city of Buffalo, has had one of the highest tuberculosis death rates in New York State. During the period 1926–1928 the average annual number of tuberculosis deaths among residents was 561, giving a mortality rate of 78.0 per 100,000 population. In 1944–1946 the average annual number of deaths among residents was 426; this figure gives a rate of 49.6 per 100,000 (1).

The tuberculosis death rate for Erie County in 1946 was 46.8 per 100,000 population. Although this rate is considerably lower than those recorded twenty years ago, it is obvious that Erie County still has excessively high mortality when one considers that in 1946 the tuberculosis death rate for the entire upstate New York area was 30.2 per 100,000 (1). With such a high death rate one might reasonably expect a high incidence of the disease. This assumption led to an examination of the local facilities available for tuberculosis case-finding in 1946.

The county has two health department clinics where individuals may obtain roentgenograms without charge. One is operated by the Buffalo City Health Department and one by the Erie County Health Service. In addition to these clinics, the city of Buffalo has several approved hospitals where chest clinics are held and where chest roentgenograms are obtainable. A chest clinic is also operated by the Buffalo and Erie County Tuberculosis Association.

In spite of these facilities, however, the city had had no concentrated drive to get the population examined roentgenographically and to find as many cases as possible, although the Tuberculosis Association had conducted several mass projects embracing some 10,000 roentgenograms over a period of three years.

The nursing services of the official health agencies did the follow-up work in connection with these projects. It became obvious, however, that more positive measures would have to be taken in order to find the unknown cases.

After study, the Board of Directors of the Buffalo and Erie County Tuberculosis Association purchased a mobile roentgenographic unit from Christmas Seal funds. On March 4, 1946, a mass tuberculosis case-finding program was undertaken for Buffalo and all of Erie County by the Tuberculosis Association. This program had the support of the Erie County Medical Society, the state and local health departments, and various other health agencies in the community.

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PLAN OF STUDY

At the beginning of the program the goal was to examine roentgenographically approximately 60,000 persons during the year (March 1946–March 1947). Actually this aim was attained in December 1946. By the end of March 1947, a period of thirteen months, 81,253 roentgenograms had been taken, an average of more than 6,000 per month. This survey was carried on in the city of Buffalo and the remainder of Erie County except for the city of Lackawanna, where a mass roentgenographic project was actively begun in April 1947.

The persons examined were distributed in all age groups and in a wide variety of occupational pursuits. As the total population of Erie County, including Buffalo, was estimated to be 869,571 on July 1, 1946 (1), it is evident that 9.3 per cent of the county's population had been examined roentgenographically by the Christmas Seal mobile unit during its first thirteen months. If only the adult population is considered, then approximately 11.1 per cent of the residents 15 years and over were examined during the thirteen month period.

Of the 81,253 roentgenograms taken, 741 proved to be unsatisfactory, duplicates, or test films. Accordingly, a total of 80,512 persons examined is used as the basis of this study.

The equipment used was a Picker unit in a tractor-trailer combination taking a 70 mm. film. All the films were developed at the clinic of the Tuberculosis Association and were read by a physician of its staff. When a tentative diagnosis of tuberculosis was made, it was based on the characteristic changes in density on the roentgenogram which are presumed to be tuberculous. Persons whose films indicated the need of further study were sent appointment letters within ten days which arranged for first follow-up examination at the office of the Association. These examinations included 14 by 17 inch roentgenograms.

The purpose of the present article is to analyze the 80,512 persons examined with 70 mm. "miniature" film during the thirteen month interval from March 4, 1946, to March 31, 1947, and to ascertain what has happened to those requested to return for follow-up examination.

OBSERVATIONS

In table 1 may be seen the total number of men and women examined by miniature film during the period studied, classified by age group.

Nearly 7 per cent of the persons examined roentgenographically were less than 15 years of age; this group is generally recognized to be unproductive so far as tuberculosis case-finding is concerned. Roentgenograms were obtained of children 12 to 14 years old only if accompanied by their parents, while those under 12 who were contacts were also examined. Subsequent tables show that very little indication of pathology appeared on the miniature films taken of children in this group.

Table 2 gives the distribution of persons examined by race, sex, and age. Since but 3,504 nonwhite persons were examined, the number was considered too small for detailed analysis.

According to table 3, 190 of the 80,512 persons examined were given preliminary diagnoses of definite tuberculosis on the miniature film, while 971 others were suspected of having the disease. For each 1,000 persons examined, 2.4 tentatively definite cases were found in addition to 12.1 suspected cases.

TABLE 1

Persons of each sex who were examined by miniature film, classified by age group: Erie County, March 4, 1946–March 31, 1947

AGE GROUP	BOTH SEXES		MALE		FEMALE	
	Number	Per cent distribution	Number	Per cent distribution	Number	Per cent distribution
All ages	80,512	100.0	38,711	100.0	41,801	100.0
Under 15 years	5,464	6.8	2,496	6.4	2,968	7.1
15 to 24 years	29,164	36.2	13,527	34.9	15,637	37.4
25 to 34 years	16,176	20.1	7,390	19.1	8,786	21.0
35 to 44 years	13,808	17.2	6,651	17.2	7,157	17.1
45 to 54 years	9,252	11.5	4,852	12.5	4,400	10.5
55 to 64 years	4,673	5.8	2,630	6.8	2,043	4.9
65 years and over	1,483	1.8	899	2.3	584	1.4
Age not reported	492	0.6	266	0.7	226	0.5

TABLE 2

White and nonwhite persons of each sex who were examined by miniature film, classified by age group: Erie County, March 4, 1946—March 31, 1947

AGE GROUP	WHITE			NONWHITE		
	Both sexes	Male	Female	Both sexes	Male	Female
All ages	77,008	37,191	39,817	3,504	1,520	1,984
Under 15 years	5,184	2,356	2,828	280	140	140
15 to 24 years	28,042	13,068	14,974	1,122	459	663
25 to 34 years	15,284	7,062	8,222	892	328	564
35 to 44 years	13,206	6,376	6,830	602	275	327
45 to 54 years	8,850	4,652	4,198	402	200	202
55 to 64 years	4,539	2,548	1,991	134	82	52
65 years and over	1,432	876	556	51	23	28
Age not reported	471	253	218	21	13	8

The interesting feature of table 3 is the fact that the proportion of cases found increases directly with the age of those examined. This statement holds whether one considers the proportion of persons with tentative diagnoses of definite tuberculosis or the proportion with suspected tuberculosis.

This table corroborates the findings of certain other studies. The success of a mass case-finding project hinges on ability to induce large numbers of older persons to be examined, though this fact is not widely recognized. The higher

the median age of the group examined, the larger will be the number of cases found.

Among the white persons examined, 2.4 per 1,000 were tentatively diagnosed as having definite tuberculosis; this proportion is the same as that for the entire group. The corresponding proportion for the nonwhite group was 1.7 per 1,000 on whom roentgenograms were obtained.

Cases considered suspicious among the white group numbered 11.9 per 1,000 examined, compared to 14.8 per 1,000 nonwhite persons.

Roentgenograms were obtained of a larger proportion of the Buffalo residents than in the remainder of the county, but the proportion of definite and suspicious cases found was slightly higher in the county.

TABLE 3

Persons examined by miniature film and number and per cent with tentative diagnoses of definite or suspicious tuberculosis, classified by age group: Erie County, March 4, 1946–March 31, 1947

AGE GROUP	PERSONS EXAMINED ROENTGENOGRAPHICALLY	PERSONS WITH TENTATIVE DIAGNOSES OF DEFINITE TUBERCULOSIS		PERSONS WITH SUSPICIOUS TUBERCULOSIS	
		Number	Rate per 1,000 persons examined	Number	Rate per 1,000 persons examined
All ages	80,512	190	2.4	971	12.1
Under 15 years	5,464	1	0.2	8	1.5
15 to 24 years	29,164	23	0.8	144	4.9
25 to 34 years	16,176	30	1.9	180	11.1
35 to 44 years	13,808	44	3.2	216	15.6
45 to 54 years	9,252	42	4.5	203	22.0
55 to 64 years	4,673	37	7.9	143	30.6
65 years and over	1,483	13	8.8	73	49.2
Age not reported	492	—	—	4	8.1

Although tentative diagnoses were made on the basis of miniature films, more definite diagnoses occurred after a follow-up examination and study. In the miniature films, tentative diagnoses of so-called definite tuberculosis were made in 190 cases, suspect tuberculosis in 971, and nontuberculous abnormalities in 383 cases. A total of 1,576 persons needing examination and second roentgenograms were invited to return to the chest clinic of the Buffalo and Erie County Tuberculosis Association. In response to this request, 1,490 persons were examined; 1,298 of these returned to the Association clinic for their first follow-up examinations and 14 by 17 films. This number includes 147 persons tentatively diagnosed as having definite tuberculosis, 811 with suspect tuberculosis, 308 with nontuberculous abnormalities, and 32 whose miniature films were unsatisfactory.

The names of those who failed to appear for this follow-up examination at the Tuberculosis Association's clinic were turned over to the health departments for

subsequent follow-up. This group was referred either to the City Chest Clinic or to the Erie County Health Service, depending upon their places of residence. There were 192 of this group examined, including 29 who were tentatively diagnosed as definite tuberculosis on the miniature film, 108 considered to be tuberculosis suspects, and 55 with nontuberculous abnormalities.

In table 4 are presented the findings on the follow-up of 1,490 persons on whom 14 by 17 films were taken at these three clinics. According to this table, a total of 335 clinically significant cases of tuberculosis was found as a result of examining 80,512 persons by roentgenogram. These figures indicate that 4.16 clinically significant cases were found per 1,000 examined. This finding is

TABLE 4

Cases diagnosed on 14 by 17 film, classified by tentative diagnosis on miniature film: Erie County, March 4, 1946–March 31, 1947

TENTATIVE DIAGNOSIS ON MINIATURE FILM	TOTAL EXAMINED BY 14 BY 17 FILM	CLINICALLY SIGNIFICANT CASES OF PULMONARY TUBERCULOSIS DIAGNOSED BY 14 BY 17 FILM				SUSPICIOUS TUBERCULOSIS	APPARENTLY CURED TUBERCULOSIS	NONTUBERCULOUS ABNORMALITIES	ESSENTIALLY NEGATIVE	EXAMINATION PENDING
		Total	Minimal	Moderately advanced	Far advanced					
All diagnoses	1,490	335	255	73	7	68	242	388	423	34
"Definitely tuberculosis"	176	118	66	45	7	5	34	10	2	7
Suspicious tuberculosis	919	212	186	26	—	55	190	128	316	18
Nontuberculous abnormalities	363	3	2	1	—	8	17	247	79	9
Cardiac condition	21	—	—	—	—	—	—	19	2	—
Suspected silicosis	16	—	—	—	—	1	—	13	1	1
Other pathology	326	3	2	1	—	7	17	215	76	8
Unsatisfactory film	32	2	1	1	—	—	1	3	26	—

comparable to that of other mass case-finding projects in which approximately 4 active cases were found per 1,000 *adults* examined.

A check of health department records revealed that 23, or approximately 7 per cent, of these 335 clinically significant cases were previously known. As stated earlier in this article, the number of cases found depends largely upon the ages of the persons examined.

In addition to the clinically significant cases of tuberculosis, 68 cases were considered to be suspicious tuberculosis, 242 were found to be apparently cured, and 388 individuals showed evidence of some nontuberculous abnormality. The last named group included instances of marked fibrosis, emphysema, pneumonia, neoplasm, or cardiac enlargment which would warrant further study.

Of the 176 cases diagnosed as "definite tuberculosis" on the miniature films two-thirds (118) were considered to be clinically significant when the 14 by 17 films were scrutinized. Moreover, 23 per cent of the 919 persons whose miniature films implied suspicious tuberculosis proved to have the disease in a clinically significant stage when the larger films had been taken.

Three-fourths (255) of the 335 clinically significant cases found in this survey were diagnosed as in the minimal stage. This percentage compares favorably with the findings of other mass case-finding projects.

A summary of the significant findings among the 80,512 persons examined is shown in table 5. It is interesting to note that the tuberculosis cases found are less numerous than are the cases with nontuberculous abnormalities.

From the data in table 5 it is evident that 1.28 per cent of the 80,512 persons examined were found to have some stage of tuberculosis or some other pathologi-

TABLE 5

Number and rate of pathological cases found per 1,000 examined, classified by diagnosis on 14 by 17 film: Erie County, March 4, 1946–March 31, 1947

DIAGNOSIS ON 14 BY 17 FILMS	PATHOLOGICAL CASES FOUND	
	Number	Per 1,000 persons examined
All diagnoses	1,033	12.83
Clinically significant tuberculosis	335	4.16
Suspected tuberculosis	68	0.84
Apparently cured tuberculosis	242	3.01
Nontuberculous abnormalities	388	4.81

TABLE 6

Persons with specified diagnoses on miniature films who had failed to return for follow-up by April 1, 1947, classified by reason for failure to appear: Erie County, March 4, 1946–March 31, 1947

REASON FOR FAILURE TO APPEAR FOR FOLLOW-UP	PERSONS WITH SPECIFIED DIAGNOSES ON MINIATURE FILM WHO FAILED TO RETURN FOR FOLLOW-UP			
	Total	"Definite tuberculosis"	Suspicious tuberculosis	Nontuberculous abnormalities
All reasons	86	14	52	20
Refused to be re-examined	47	5	29	13
Under care of private physician	20	7	12	1
Could not be located	17	1	11	5
Returned to tuberculosis sanatorium	2	1	—	1

cal condition. If the apparently cured group is disregarded, then one per cent of those examined roentgenographically needed further supervision. A report was sent in each instance to the patient's private physician.

In surveys of this size it is impossible to obtain 100 per cent follow-up. For example, 86 persons failed to appear who were supposed to report for follow-up after their miniature films had been read. The names of these persons were referred to the city health department and were checked by public health nurses.

In table 6 may be seen the reasons for failure to return for follow-up examinations, together with the initial diagnoses on the miniature films. As 1,576 were requested to return and only 47 definitely refused to do so, it is evident that the

uncooperative group was but 3 per cent of those who needed follow-up. It is difficult to determine whether the group which could not be located were uncooperative or not.

SUMMARY AND CONCLUSIONS

Between March 4, 1946 and March 31, 1947, a mass case-finding project was carried on in Erie County, New York by the Buffalo and Erie County Tuberculosis Association. During this period 80,512 persons had chest roentgenograms (miniature films) and 1,576 were found to need further study. The first step in this follow-up procedure consisted of examination and another roentgenogram on a 14 by 17 film.

The Tuberculosis Association carried on this intensive follow-up work leading to examination and the obtaining of 14 by 17 roentgenograms of those individuals requiring review. As a result, 335 persons, or 4.16 per 1,000 examined, were found to have clinically significant tuberculosis. Three-fourths of these 335 were minimal cases, an indication that their chances of recovery are excellent. Presumably the majority of these minimal cases would not have become known at this time unless the mass survey had been held. A check of health department records revealed that 23, or approximately 7 per cent, of the 335 clinically significant cases had been previously reported.

In addition to the 335 cases of tuberculosis which were found, 388 diagnoses of nontuberculous abnormalities were made as a result of the survey. This finding must be considered as of equal importance to the discovery of 335 cases of tuberculosis.

One of the most significant results of this study is the finding that the proportion of cases discovered increases directly with the age of the persons examined.

If one considers all types of pathological cases found among the 80,512 persons examined, it becomes apparent that one per cent of the entire group presents some abnormality requiring medical attention.

A mobile chest roentgenographic service should continue to be a valuable component of any over-all tuberculosis control program. The Erie County, New York, experience demonstrates clearly how such a mobile unit can be coordinated effectively with the official health agencies and other community organizations and facilities.

SUMARIO

Obra de Descubrimiento de Casos de Tuberculosis

Del 4 de marzo de 1946 al 31 de marzo de 1947 se llevó a cabo una obra colectiva de descubrimiento de casos en el Condado Erie, en el Estado de Nueva York, por la Asociación Anti-Tuberculosa de la ciudad de Búffalo y el Condado Erie. Durante dicho período de tiempo, obtuviéronse radiografías torácicas (películas en miniatura) de 80,512 personas, en 1,576 de las cuales se observó la necesidad de estudio más detenido. El primer tiempo en este procedimiento de observación ulterior consistió en un examen y otra radiografía de 35 por 52.5 cm.

La Asociación Anti-Tuberculosa ejecutó esta obra intensa de observación con el examen y la obtención de películas mayores en los individuos que exigían repaso, como resultado de la cual se descubrió que 335 personas, o sea 4.16 por cada 1,000 examinados, mostraban tuberculosis de importancia clínica. Tres cuartas partes de las 335 tenían casos mínimos, indicando esto excelentes probabilidades de curación. Es de presumir que la mayoría de dichos casos mínimos no hubieran sido conocidos para aquella fecha, de no haberse verificado la encuesta colectiva. El estudio de los archivos del departamento de sanidad reveló que 23, aproximadamente 7 por ciento, de los 335 casos clínicamente significativos habían sido denunciados anteriormente.

Además de los 335 casos tuberculosos descubiertos, se hicieron, a consecuencia de la encuesta, 388 diagnósticos de anomalías no tuberculosas, hallazgo este que debe considerarse igual en importancia al descubrimiento de los casos tuberculosos.

Uno de los resultados más importantes de este estudio consiste en la observación de que la proporción de casos descubiertos aumenta en razón directa a la edad de las personas examinadas.

Tomando en cuenta todas las formas de patología observadas entre las 80,512 personas examinadas, resulta evidente que uno por ciento del grupo completo presentaba alguna anomalía que exigía asistencia médica.

Un servicio movible de radiografía torácica debe continuar formando un valioso componente de toda obra general de lucha antituberculosa. Lo observado en el Condado Erie demuestra claramente la forma en que una unidad movible como la descrita puede coordinarse eficazmente con los organismos oficiales de sanidad y con otros organismos y recursos cívicos.

Acknowledgments

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REFERENCES

(1) Population in 1946 and resident tuberculosis deaths all forms, and rates per 100,000 population, by counties, and certain cities in upstate New York for 1926–1928, 1944–1946 and 1946, with percentage decline in rates, Bulletin, N. Y. State Dept. of Health, Division of Tuberculosis, April 15, 1947, page 1.

THE ISOLATION OF THREE DIFFERENT PROTEINS AND TWO POLYSACCHARIDES FROM TUBERCULIN BY ALCOHOL FRACTIONATION. THEIR CHEMICAL AND BIOLOGICAL PROPERTIES[1,2]

FLORENCE B. SEIBERT

INTRODUCTION

Previous studies (1) have shown that the protein moiety of tuberculin is a complex mixture of proteins. The conclusions reached in those studies were based upon researches on fractions isolated from heated tuberculin. Such fractions must have been mixtures of proteins denatured by heat and undenatured proteins that withstood the heat. It was decided, therefore, that a more logical approach to the study of the proteins could be made by fractionating raw unheated tuberculin and later, if desired, denaturing the isolated fractions.

The following outline represents a compilation of the methods which have proved to be most successful in fractionating the tuberculin component into electrophoretically distinguishable substances. No attempt is made to describe in detail each of the many complete fractionations that were made. Complete data are available in files in this laboratory. Only those steps are given which were finally chosen as most desirable after numerous modifications, and it is recognized that the scheme of fractionation here outlined should be considered preliminary. It is presented at this time because it may lead to the development of a more specific tuberculin than has been available previously and because it might be helpful to other investigators in this field.

It will be shown below that the following components of tuberculin were isolated: two distinct polysaccharides, designated I and II; and three distinguishable proteins, designated A, B and C. These proteins have also been discussed previously (1). The A protein had the slowest migration when studied in electrophoresis, and the B and C proteins had a faster migration. While the mobilities of the B and C proteins were approximately the same, their solubility properties were different. Polysaccharide I was the small polysaccharide molecule studied extensively in the past (1, 2), and polysaccharide II was a large molecule not hitherto described and found in quantity only in culture filtrates of certain strains of tubercle bacilli.

OUTLINE OF FRACTIONATION PROCEDURE

Growth of bacilli: Tubercle bacilli of the following strains, human DT, H 37 and A 33, and bovine BCG were grown on Long's synthetic medium, usually for eight to twelve weeks. In the case of one fractionation (No. 99) the bacilli were grown for only five weeks, and in another (No. 96) for thirteen weeks.

[1] From The Henry Phipps Institute, University of Pennsylvania, Philadelphia.

[2] Aided by grants from the Committee on Medical Research of the National Tuberculosis Association.

Harvesting of bacilli: The bacilli were filtered off, without previous heating of the culture, through large Seitz filters as quickly as possible. The filtrates were removed to a cold room held at 1 to 2°C and all subsequent procedures were carried out at this temperature, using no preservative.

Concentration of the filtrate and washing: The filtrates were concentrated by means of ultrafiltration through 9 per cent[3] gun cotton membranes, as described previously (3), to a tenth or a hundredth of the original volume, depending upon the viscosity of the solutions. Toward the end of the concentration water was added and the ultrafiltration continued in order to reduce the salt content of the solutions, as better fractionation occurred when the precipitations were made in the presence of a low salt concentration.

Precipitation of C protein: The C protein was precipitated by adjusting the concentrated ultrafiltrates to pH 3.8 to 4.7 by slowly adding acetic acid with stirring. The precipitates, which were colored a moderate yellow, were centrifuged off and washed with acetate buffer pH 4.0, $\mu = 0.02$. Further purification can be effected by redissolving and reprecipitating.

Fractionation of the supernatant: The supernatants, after removal of the C protein at about pH 4.0, showed in electrophoresis (see figure 4) the presence of two main protein components, designated as A and B proteins. In some cases there was present also a considerable amount of polysaccharide with very low mobility, as can be seen in the last two diagrams of figure 4.

Separation of the A and B proteins was at first attempted by means of ammonium sulfate fractionation, as small amounts of relatively pure A protein had previously been obtained in this way (4, 5). But after repeated trials, using one-fourth, one-third or one-half saturated ammonium sulfate at either pH 4.0 or pH 7.0, it was concluded that this method of separation was not satisfactory.

Therefore, electrophoretic separation was considered. This method is possible only when the resolution of the components is sufficiently sharp to yield distinct components, as in the case of the second supernatant shown in figure 4. The results of fractionation of this supernatant (lot No. 84) will be described later. In the great majority of cases, however, this method is not advisable.

Finally, alcohol fractionation was attempted and proved to be superior to any methods so far used. The steps in the procedure found to be most successful are given below. Although the fractionations were made at a temperature of 1°C, a lower temperature (-5° to -10°C) would be desirable in order to reduce the possibilities of denaturing the proteins.

Precipitation of polysaccharide II: The supernatant, after precipitation of the C protein at pH 4.0, was brought back to neutrality by slow addition of weak alkali while stirring. In cases where the solution was not clear it was filtered through the Seitz filter. It was then concentrated on fresh ultrafilters to a small volume. To this solution was added sufficient 95 per cent alcohol with stirring to give a 30 per cent alcohol concentration. A white gelatinous precipitate occurred which dissolved slowly in water, giving a white opalescent solution which appeared blue in dim light. It was named polysaccharide II to distinguish it from the polysaccharide previously described (1, 2) and now called polysaccharide I.

Precipitation of protein B: The supernatant from polysaccharide II, which had a pH of 7.0 and an alcohol concentration of 30 per cent, was readjusted to about pH 4.6 by

[3] Nine per cent gun cotton, as now available, gives a porosity which was given previously by 11 per cent.

addition of acetic acid with stirring and a precipitate, consisting chiefly of protein B, came out.

Precipitation of protein A: After removal of the B protein at about pH 4.6 with 30 per cent alcohol, more alcohol was added to the supernatant to give a concentration of 70 per cent. The resulting precipitate contained chiefly the A protein.

Recovery of polysaccharide I from final residue: After the A protein was removed, the supernatant was dialyzed to remove alcohol and then concentrated by ultrafiltration. Any trace of protein was precipitated by trichloracetic acid and removed. The supernatant was again dialyzed to free it from trichloracetic acid and the remaining solution contained polysaccharide I.

TABLE 1

Yields of proteins and polysaccharides isolated from different preparations of tuberculin

LOT NUMBER OF PREPARATION	STRAIN* OF TUBERCLE BACILLUS	VOLUME OF LONG'S MEDIUM INOCULATED	POLYSACCHARIDE I	POLYSACCHARIDE II	PROTEIN A	PROTEIN B	PROTEINS A + B	PROTEIN C
		Liters	*Gm.*	*Gm.*	*Gm.*	*Gm.*	*Gm.*	*Gm.*
84	DT	14	0.6				0.7	0.4
88	DT	20	0.4				0.6	0.7
90	DT	20	2.8				1.1	2.5
92	H37	19	0.7?	4.7			1.5	2.0
93	H37	4.5		3.6			1.2	0.8
94	DT	10	0.9				0.6	3.4
95	BCG	40	0.4	0.2			2.4	1.1
96A	A33	24.5	1.0	0.7	1.7	0.32		6.3
96B	A33	9.4	0.2+	0.1			0.4	1.5
98	DT	36	0.5	0.1	0.9	2.7		4.7
99	DT	35			0.025	0.03		0.2

* All strains were human type tubercle bacilli except BCG.

EXPERIMENTS

Yields of Components Isolated

Table 1 shows the amounts of the different proteins and polysaccharides actually isolated during each fractionation. No claim is made that the maximum yield of any of the products was obtained. During these experiments the proper conditions for isolation were being sought and the losses were necessarily great. This is especially true in the case of polysaccharide I. The yields do, however, give a rough idea of the relative amounts of the different components present and they show that in most cases the C protein constituted a large portion of the total yield.

Electrophoretic Analyses of the Isolated Fractions and Components

All electrophoretic analyses were carried out in phosphate buffer pH 7.7, $\mu = 0.1$, at a potential gradient of 9 to 10 volts per cm. The ranges of the mobilities[4] of the isolated components are shown in table 2. When purer fractions

[4] All mobilities are recorded in units of 10^{-5} cm.^{2} volt^{-1} sec.$^{-1}$.

are obtained these ranges undoubtedly will become narrower. Characteristic properties important in the isolation of these components are also given in table 2.

Concentrated original ultrafiltrates: Examination of small samples of the original filtrates by means of electrophoresis afforded a quick method for revealing the relative proportions of the different components present (figure 1). It can be seen, for example, that the filtrates from lots Nos. 84, 98 and 99, all made from the human strain DT, contained relatively more of the faster migrating components, the proteins, than did the filtrates from lots Nos. 92 and 96A, made respectively from the H 37 and A 33 human strains. The latter two filtrates, on the other hand, contained a very large proportion of the slowly migrating components, which have proved to be the polysaccharides.

New components are also readily revealed by means of these electrophoresis analyses. For example, the diagram of the filtrate of lot No. 99 (figure 1)

TABLE 2

Electrophoretic mobilities, solubilities and conditions of precipitation of the isolated proteins and polysaccharides

COMPONENT	*MOBILITY $\times 10^{-5}$ CM^2, VOLT^{-1} SEC^{-1}	SOLUBILITY AT pH 3.8-4.7	CONDITIONS FOR PRECIPITATION
Protein			
A	−3.4 to −3.8	soluble	70 per cent alcohol, pH 4.6
B	−5.4 to −6.4	soluble	30 per cent alcohol, pH 4.6
C	−6.1 to −7.3	insoluble	acetic acid, pH 4.0
D	−8.6	insoluble	acetic acid, pH 4.0
Polysaccharide			
I	−1.4 to −2.0	soluble	95 to 100 per cent alcohol
II	−1.4 to −1.6	soluble	30 per cent alcohol, pH 7.0

* Mobilities in phosphate buffer, pH 7.7, $\mu = 0.1$, and potential gradient of 9 to 10 volts per cm.

showed a significant amount of a component which migrated with a greater velocity than the proteins. As the only difference between this filtrate and several other filtrates from the same (DT) strain, as well as from other strains, was that the culture was only five weeks old, in contrast to the eight to ten weeks of usual growth, it is possible that this component may be characteristic of early growth. Its nature will be discussed below under protein C.

Protein C: This protein was always readily precipitated at a pH 3.8 to 4.7 and even after a single precipitation showed one main electrophoretic component with a mobility of −6.1 to −7.3. Figure 2 shows diagrams of six such protein preparations isolated from the culture filtrates of four different strains of tubercle bacilli.

The fraction which precipitated at pH 4.5 from the culture filtrate (lot No. 99) of only a five weeks old culture of tubercle bacilli, strain DT, contained, in addition to C protein with mobility of −6.4, another component with a greater mobility, −8.6 (figure 3). This mobility is characteristic of nucleoproteins and

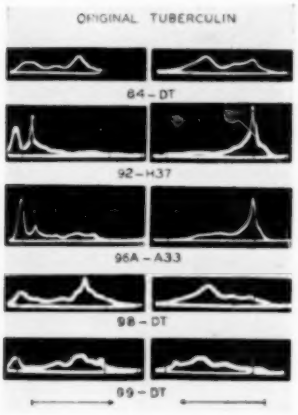

FIG. 1. Electrophoretic diagrams of six samples of concentrated original tuberculins. The diagrams on the right represent the descending patterns and those on the left the ascending patterns. After about two hours electrophoresis the components are migrating in the directions indicated by the arrows, those with the fastest mobilities occupying the positions toward the heads of the arrows. The anomalous conductivity boundaries, δ and ϵ, which are the slowest boundaries seen on either side toward the end of the arrows, are larger on the ascending side (δ) and relatively inconspicuous on the descending side (ϵ). Often the polysaccharides separate very poorly or not at all from these boundaries.

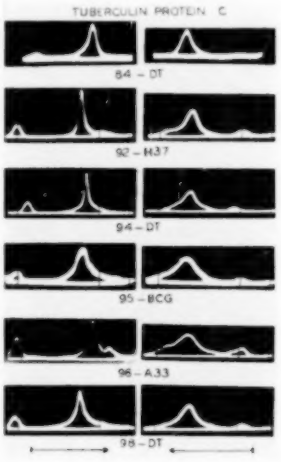

FIG. 2. Electrophoretic diagrams of six isolated C proteins which appear as the main components on both ascending and descending patterns.

it may be significant that this component appeared only in considerable quantity in the young cultures. It has been designated D component.

Supernatant from C protein, containing A and B proteins: After the C protein was removed at about pH 4.0, there remained in solution the polysaccharides and some soluble proteins, which when examined by electrophoresis appeared to consist of two proteins. One of them had nearly the same mobility as the C protein and was called B protein. The other one migrated more slowly and was called

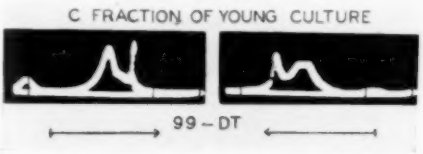

FIG. 3. Electrophoretic diagrams of the C fraction isolated from a young culture, showing the extra D component as the faster component above the head of the arrows.

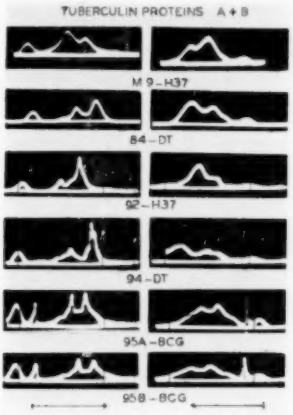

FIG. 4. Electrophoretic diagrams of six supernatant fractions after removal of the C protein. In each case the two proteins, B and A, are seen as the two fastest components. In the last two diagrams an additional slow component appears as a sharp peak with slowest mobility, next to the anomalous δ and ϵ boundaries, with no mobility. These are the polysaccharide II.

A protein (figure 4). These same proteins were found six different times and in filtrates from three different strains of tubercle bacilli.

Protein B. This protein was isolated in two different ways, as described above under the fractionation procedure.

Separation by electrophoresis. When the resolution in electrophoresis of the A and B proteins was good, as in the case of the supernatant from lot No. 84 (figure 4), the B protein was isolated by removing mechanically the faster migrating component in the ascending limb of the electrophoresis cell. It was sent to Mrs. Ellen Bevilacqua at the University of Wisconsin for sedimentation and diffusion determinations. The results were reported in her thesis (6) and showed

that it was homogeneous in both sedimentation[5] and diffusion, with the following constants, S = 2.0, D = 9.6, and a/b ratio of 5.0, and a molecular weight of about 20,000. The sedimentation constant corresponds with that found for the faster migrating protein separated by electrophoresis in an earlier study (4).

Separation by alcohol precipitation. After precipitation of the C' protein at 4.0, polysaccharide II was precipitated by 30 per cent alcohol from the supernatant which had been adjusted to a neutral reaction (see above under procedure). When this polysaccharide II was also removed, the clear supernatant,

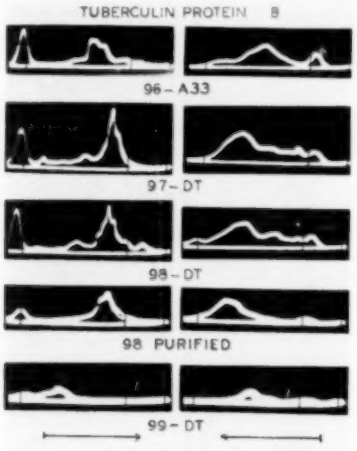

FIG. 5. Electrophoretic diagrams of five isolated B protein fractions. The B proteins appear as the conspicuous faster components. The smaller slower components are A protein and polysaccharides, and the occasional small fastest one is the D component.

containing 30 per cent alcohol, was again readjusted back to about pH 4.6 and a fraction containing mostly protein B precipitated. Fractions with similar mobilities were isolated four different times and from two different strains of tubercle bacilli, as may be seen in figure 5. In all cases the largest component represents B protein and in most cases the diagrams show also the presence of a smaller amount of a component or components migrating at a slower rate than the B protein. These components are probably the A protein and polysaccharides. Therefore, in one case (lot No. 98) where there was sufficient material available, further purification was undertaken. The entire procedure for isolation was repeated and the resulting product did show the presence of only very little of the contaminating components (figure 5, diagram marked "98 purified").

[5] Sedimentation constants (S) are recorded in units $\times 10^{-13}$, and diffusion constants (D) in units of $\times 10^{-7}$.

Protein A: This protein also has been isolated in two different ways, viz., by (1) electrophoresis, and (2) alcohol fractionation.

Separation by electrophoresis. When the supernatant remaining after the removal of the C protein was subjected to electrophoresis, the fraction migrating with the slowest mobility remained behind on the descending side and could easily be withdrawn. This fraction contained the protein with the slowest mobility, which is called protein A, and also the slowly migrating polysaccharides. When studied by Mrs. Bevilacqua (6) in the ultracentrifuge it also proved to be heterogeneous and gave evidence of at least two components, for one of which a sedimentation constant of S = 1.8 was calculated.

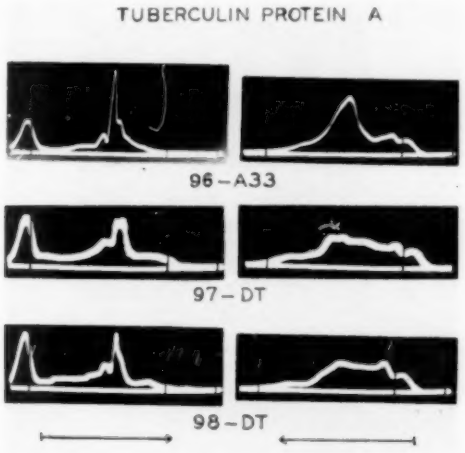

FIG. 6. Electrophoretic diagrams of three isolated A protein fractions. The conspicuous components represent the A proteins. The descending diagrams show also the presence of a considerable amount of slower components, the polysaccharides.

Separation by alcohol fractionation. After removal of the B protein fraction (see above) the supernatant had a pH of about 4.6 and an alcohol concentration of 30 per cent. The alcohol concentration was then increased to 70 per cent, as described under procedure, and a fraction containing most of the A protein precipitated (figure 6). In this precipitate only a trace of the faster migrating protein, B, was present, but there were considerable amounts of the very slowly migrating polysaccharides. Further purification of this fraction is, therefore, desirable but has so far not been possible because of lack of material.

This fraction when dissolved in water gave clear colorless solutions. It is possible that the A protein is the protein with molecular weight about 35,000 to 42,000 (4, 5) and it may also be the one which was crystallized (7), but further data will be necessary to establish such identity.

Polysaccharide II: This polysaccharide has not hitherto been described and appeared in considerable quantity only in the culture filtrates of certain strains

of tubercle bacilli, *viz.*, the H 37, A 33 and BCG strains. Its chemical and biological properties will be described in another publication. When present it could be distinguished by the opalescence which it gave to the culture filtrates. It was

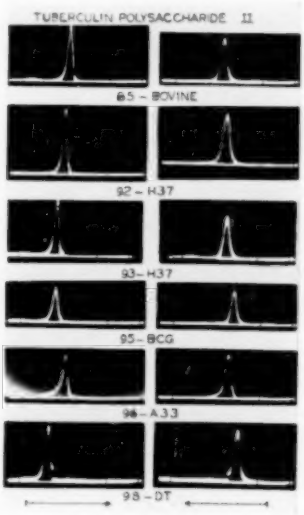

FIG. 7. Electrophoretic diagrams of six isolated polysaccharide II preparations taken after four hours of electrophoresis. No other component appeared.

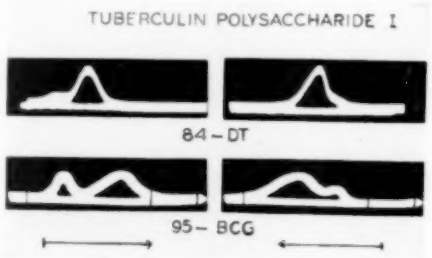

FIG. 8. Electrophoretic diagrams of two isolated polysaccharide I preparations. The δ and ε boundaries are the slower inconspicuous boundaries in the first pattern and the more definite slower peaks in the second pattern.

readily precipitated by 30 per cent alcohol at neutrality from the supernatant of the C protein, as described above. When studied in electrophoresis (figure 7) it appeared to be homogeneous, even after being subjected to the current for four hours. It has been isolated six times from the filtrates of five different strains of tubercle bacilli and its presence was apparent in the original concentrated culture

filtrates as the sharp peak with very low mobility, which can be seen in the electrophoretic diagrams of lot No. 92 H 37 and lot No. 96 A–A 33 in figure 1.

Polysaccharide I: After all of the above proteins and polysaccharide II were removed from the culture filtrate, the residue contained a considerable amount of this polysaccharide (1). It could be isolated as described above under fractionation procedure. It was the highly soluble polysaccharide of low molecular weight (7,000 to 9,000) which had been studied extensively and whose properties have been reviewed previously (1, 2). The electrophoretic diagrams are shown in figure 8. In most cases it would be possible to isolate considerably more of this component than is reported in table 1.

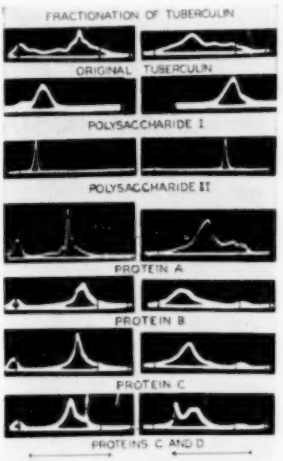

FIG. 9. Electrophoretic diagrams of a typical original concentrated tuberculin and below it the isolated fractions corresponding to those distinguishable in the original diagram. As all pictures were taken after approximately the same time of electrophoresis, their positions indicate their relative rates of migration. The sizes of the components do not correspond with the relative concentrations present in the original tuberculin.

Figure 9 shows an electrophoretic diagram of an original concentrated tuberculin and below it patterns of isolated components with mobilities corresponding to those distinguishable in the original composite diagram.

Chemical Analyses

Methods. The content of polysaccharide was determined by means of the carbazole reaction (8, 9), using the purest polysaccharide I or polysaccharide II as standard.

Nucleic acid was determined by means of the Dische diphenylamine reaction (8, 10), using Hammarsten's sodium thymus nucleate as standard.

Both carbohydrate and nucleic acid contents were calculated in relation to a simultaneous concentration of 1 mg. per ml. of protein in the same solutions.

The spectral absorption in ultraviolet light was measured with a Beckman spectro-

photometer—U V, and the specific densities were calculated on the basis of a protein concentration of 1 mg. per ml. The protein contents were determined from the nitrogen contents.

TABLE 3

Polysaccharide and nucleic acid analyses and spectral densities of tuberculin proteins, A, B and C.

TYPE OF PROTEIN	LOT NUMBER	POLYSACCHARIDE	NUCLEIC ACID	SPECIFIC SPECTRAL DENSITY AT		RATIO $D_{\lambda 2800}/D_{\lambda 2500}$	TUBERCULIN SKIN POTENCY RELATIVE TO PPD-S IN HUMAN BEINGS
				λ 2800 Å	λ 2500 Å		
		mg. per ml.	*mg. per ml*				
A + B	90			1.18	0.39	3.1	>
A + B	92			2.01	0.75	2.7	
A + B	93			1.07	0.54	2.0	
A + B	94			1.36	0.56	2.5	>
A + B	95	0.154	0.0026	1.01	0.48	2.1	>
A	96A*		0.0017	2.07	0.79	2.6	<
A	96B*		0.0100	1.29	0.59	2.2	>[x]
A	97		0	1.52	0.48	3.2	>[x]
A	98	1.420	0.0106	1.34	0.58	2.3	=
A + B	99‡		0.0090	0.74	0.41	1.8	>[x]
Average				1.36	0.56	2.5	
B	96A*		0.0053	0.88	0.47	1.9	<[x]
B	97		0.0060	1.42	0.70	2.0	>[x]
B	98			1.39	0.70	2.0	>[x]
Average				1.85	0.94	2.0	
C	90			2.14	1.54	1.4	
C	92			1.34	0.87	1.5	<
C	93			1.58	1.11	1.4	
C	94			1.79	1.41	1.3	<
C	95	0.070	0.0067	1.69	1.21	1.4	<
C	96A*		0.0545	2.08	1.80	1.2	<
C	96B*		0.0040	1.37	0.90	1.5	>[x]
C	98	0.034	0.0035	1.92	1.50	1.3	<
C + D	99‡		0.0070	0.99	0.51	1.9	<[x]
Average				1.64	1.20	1.4	

* Lots 96 A and B were made from thirteen week old cultures and the A protein was precipitated with trichloracetic acid instead of acetic acid.

‡ These fractions were made from a five weeks old culture filtrate. See text.

[x] These tests were made in tuberculous guinea pigs rather than in human beings.

Results: The concentrations of nucleic acid and of carbohydrate are recorded in table 3. The few analyses available show a higher content of polysaccharide with the A and A + B proteins than with the C proteins, as would be expected. The content of nucleic acid was very low in all cases, but as there may be an error

when the diphenylamine reaction is used in the presence of much protein, further work must be done before a definite statement can be made concerning the exact content of nucleic acid in these fractions.

The specific spectral maximum and minimum densities in the ultraviolet light, as well as the ratios of the maximum to the minimum densities, are recorded in table 3. The maximum absorption was at a wave length of 2,800 Å, except in a few cases of the C protein, where it was at a wave length of 2,700 Å, and minima were in all cases at a wave length of 2,500 Å. It is apparent from table 3 that, whereas the maximum specific densities at a wave length of 2,800 Å were nearly the same for all A or C proteins, there was considerable difference between the A and C proteins in the amount of specific density at their minima, *i.e.*, at a wave

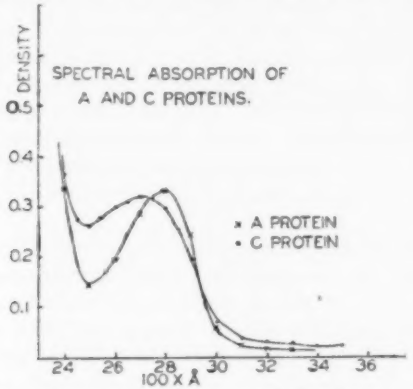

FIG. 10. Spectral absorption curves of the A and C proteins, measured with a Beckman spectrophotometer in the ultraviolet region. The concentrations chosen were such as to give practically equivalent densities at a wave length of 2800 Å, in order to show the relative difference in densities at 2500 Å.

length of 2,500 Å. This is illustrated by one set of curves given in figure 10. This difference caused a large difference in the ratios of density at 2,800 Å/2,500 Å for the A and C proteins, and means that there is something in the C proteins which has about twice as great an absorption capacity at a wave length of 2,500 Å as in the A proteins. The presence in the C proteins of a substance such as nucleic acid, with its maximum absorption at a wave length of 2,600 Å could be responsible for this effect, as well as for causing the maximum to shift from a wave length of 2,800 Å to 2,700 Å. Such a nucleoprotein would also have a higher electrophoretic mobility, similar to that found for the C proteins.

Tuberculin Potency of the Proteins and Polysaccharides

The tuberculin potencies of the isolated proteins, given in equivalent dosages in 0.1 ml. based on the nitrogen contents, were compared in tuberculous guinea pigs and in tuberculin-positive human beings. The size of skin reaction elicited by the proteins was compared with that caused by an equal dosage, based on the

nitrogen content, of the PPD-S, which is the tuberculin adopted as standard in the United States (3). In some cases only one product was compared on the same guinea pig with the standard, and in other cases three or more proteins were simultaneously injected with the standard. The results are given in table 4. All reactions were read twenty-four hours following the tests and these reactions were recorded in the top lines in the table. Readings were also made at forty-eight hours and those reactions recorded in the lower lines.

The results of the multiple test procedure showed that the A proteins always caused larger reactions than did the C proteins, while usually the B proteins gave reactions of intermediate size. When the A and C proteins alone were compared with each other, the A was again the more potent.

When tested in sensitive human beings in a dosage of 0.00002 mg., the A + B proteins were more potent than the PPD-S, and the C proteins less potent. However, when tested in less sensitive individuals in a dosage of 0.005 mg., the A + B proteins were more potent than the PPD-S and the reactions to the C proteins were as great or greater than with the PPD-S, in spite of the fact that some reactions were even missed with it. These reactions have been reported in another paper (11). This was interpreted to mean that the C protein was less specific and the A protein more specific than the whole mixture of proteins existing in PPD-S.

Neither of the polysaccharides gave skin reactions in tuberculous animals or human beings. This was the conclusion reached by Watson (2, 12) with regard to polysaccharide I. In the present study it was found that polysaccharide II also elicited no reaction in tuberculous guinea pigs nor (even with 0.05 mg. dose) in sensitive human beings who gave definite tuberculin reactions with 0.00002 mg. PPD-S.

DISCUSSION

The indication that the A protein might give more specific tuberculin reactions than the other proteins in tuberculin is sufficient reason for further endeavor to obtain this protein in highly purified form. It has been shown in these studies that the A type of protein is the most potent in causing the tuberculin skin reaction and this confirmed the earlier finding (4) that that protein fraction in crude tuberculin which migrated with the slowest mobility was the most potent one in both the skin test and the lethal test in tuberculous guinea pigs.

In view of the statement by Lind (13) that a more potent PPD could be made from young than from old cultures, it was hoped that it might be possible to isolate relatively more of the A type of protein from such cultures. This was not found to be the case, however, as shown in the yield of A protein isolated from the filtrate of lot No. 99 (see table 1), nor were any of the isolated fractions relatively more potent than similar protein fractions obtained from older cultures. As a matter of fact, all components were isolated from this five-week-old culture filtrate in relatively the same proportion as from older cultures of the same strain (DT), but in insignificant amounts. The only difference found was the notable presence of the component (D) which migrated with a high velocity, suggestive

TABLE 4

Comparison of skin reactions in guinea pigs with different tuberculin proteins

CONDITION OF GUINEA PIGS	NUMBER OF GUINEA PIGS TESTED	DOSAGE	AVERAGE DIMENSIONS OF REACTIONS IN MILLIMETERS WITH				
			PPD-S	A (Lot 98)	B (Lot 98)	B (Purified) (Lot 98)	C (Lot 98)
		mg.					
Normal	2	0.005	0 0	0 0	0 0	0 0	0 0
BCG	3	0.005	18 x 22 x 2.3 19 x 22 x 3.0	27 x 38 x 3.3 21 x 31 x 3.0	25 x 30 x 2.6 22 x 22 x 3.0	28 x 29 x 3.0 21 x 25 x 3.0	20 x 20 x 2.6 20 x 21 x 3.0
Normal	2	0.0005	0 0	0 0	0 0	0 0	0 0
Tuberculosis	3	0.0005	18 x 21 x 2.7 16 x 16 x 2.7	26 x 32 x 3.0 23 x 24 x 3.7			
Tuberculosis	4	0.0005	23 x 31 x 3.0 21 x 19 x 2.7			29 x 35 x 3.7 23 x 25 x 3.3	
Tuberculosis	3	0.0005	18 x 23 x 2.7 18 x 18 x 2.7				22 x 23 x 3.0 20 x 22 x 3.3
Tuberculosis	2	0.0005	14 x 17 x 2.0 17 x 19 x 2.6	20 x 22 x 3.0 23 x 24 x 3.7		15 x 20 x 2.6 18 x 19 x 3.0	11 x 13 x 1.3 13 x 13 x 2.0
Tuberculosis	3	0.0005		21 x 22 x 3.0 22 x 23 x 3.7			15 x 15 x 2.3 15 x 17 x 2.3
			PPD-S	A (Lot 99)	B (Lot 99)		C (Lot 99)
Normal	2	0.0005	0 0	0 0	0 0		0 0
Tuberculosis	3	0.0005	14 x 18 x 2.3 14 x 16 x 2.0	21 x 24 x 3 19 x 24 x 3			
Tuberculosis	3	0.0005	18 x 20 x 3.0 19 x 19 x 3.0		17 x 21 x 3.0 15 x 18 x 3.0		
Tuberculosis	3	0.0005	21 x 24 x 3.0 17 x 17 x 3.0				22 x 26 x 3.0 15 x 18 x 2.7
Tuberculosis	2	0.0005	21 x 23 x 3.0 20 x 18 x 3.0	22 x 25 x 3.0 21 x 22 x 3.0	20 x 21 x 3.0 19 x 19 x 3.0		18 x 19 x 2.5 17 x 18 x 2.0
			PPD-S	A (Lot 97)	B (Lot 97)		
Normals	2	0.00025	0 0	0 0	0 0		
Tuberculosis	4	0.00025	17 x 17 x 2.5 16 x 17 x 2.5	19 x 20 x 3.3 18 x 20 x 2.8	22 x 23 x 3.3 20 x 22 x 3.3		
			PPD-S	A (Lot 96A)	B (Lot 96A)		C (Lot 96A)
Normals	2	0.00025	0 0	0 0	0 0		0 0
Tuberculosis	4	0.00025	19 x 20 x 3.0 17 x 17 x 3.0	21 x 23 x 3.2 19 x 21 x 3.0	18 x 19 x 3.0 15 x 16 x 2.5		17 x 18 x 2.7 15 x 17 x 2.5
			PPD-S	A (Lot 96B)			C (Lot 96B)
Normals	2	0.00025	0 0	0 0			0 0
Tuberculosis	4	0.00025	16 x 18 x 2.3 14 x 15 x 2.3	20 x 22 x 3.3 19 x 21 x 3.0			19 x 21 x 2.5 14 x 16 x 2.3

of nucleoprotein. The C protein fraction which contained this component (figure 2) was also not significantly more potent than other C proteins. It is interesting in this connection that Heilman (14) noted also that the protein associated with nucleic acid was relatively less potent as a specific cytotoxic agent.

SUMMARY

A preliminary procedure, utilizing fractionation with alcohol at low temperature, has been presented for isolating from raw unheated tuberculin, made by growing different strains of tubercle bacilli on synthetic medium, two different polysaccharides (designated I and II) and three different proteins (designated A, B, and C).

Each of these components, all of which have been isolated several times and from the culture filtrates of different strains of tubercle bacilli, can be identified by its electrophoretic mobility. In the order of increasing mobility they were polysaccharides I and II, proteins A, B, and C.

A component with a still greater mobility, designated as D and possibly a nucleoprotein, was found to exist in significant amount in a five-week-old culture but not in older cultures from the same strain or other strains of tubercle bacilli.

Different strains of tubercle bacilli yielded different relative amounts of the polysaccharide and protein components. The amounts could be predicted from the electrophoretic diagrams of the original concentrated tuberculin filtrates.

Protein A was more potent and possibly more specific than protein C in eliciting the tuberculin skin reaction in infected animals and human beings.

The A and C proteins had similar spectral specific densities in ultraviolet light at a wave length of 2,800 Å, but the C proteins had nearly twice the specific densities at a wave length of 2,500 Å, giving a density ratio $\left(\frac{\lambda\ 2800}{\lambda\ 2500}\right)$ of about half that for the A proteins. Utilization of this ratio may help in the identification of A and C proteins during a fractionation.

SUMARIO

Aislamiento por la Fraccionacion con Alcohol de Tres Distintas Proteínas y Dos Polisacáridos de la Tuberculina, con las Propiedades Quimicas y Biologicas de los Mismos

Describese un procedimiento preliminar, que utiliza la fraccionación con alcohol a baja temperatura, para aislar de la tuberculina bruta no calentada (obtenida cultivando en medio sintético diversas cepas de bacilos tuberculosos) dos distintos polisacáridos (designados I y II) y tres diversas proteínas (denominadas A, B y C).

Cada uno de dichos componentes, todos los cuales han sido aislados varias veces y de los filtrados culturales de diversas cepas tuberculosas, puede ser identificado por su movilidad electroforética, figurando en el orden de su mayor movilidad los polisacáridos I y II y las proteínas A, B y C.

Otro componente, dotado aun de mayor movilidad, y denominado D, posible-

mente una núcleoproteína, se encontró en cantidad significativa en un cultivo de cinco semanas, pero no en los cultivos más viejos de la misma cepa ni en otras cepas de bacilos tuberculosos.

Acknowledgment

The writer wishes to express her appreciation to Dr. J. W. Williams for discussions concerning methods of alcohol fractionation and to Mrs. Ellen Bevilacqua for the sedimentation and diffusion determinations made in Doctor Williams's laboratory.

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A COMPARISON OF THE IMMUNOGENICITY FOR GUINEA PIGS OF BCG CULTURED INTERMITTENTLY AND CONTINUOUSLY IN THE PRESENCE OF BILE[1]

IRWIN S. NEIMAN AND NELDA HOLMGREN

INTRODUCTION

In their well-known textbook, Topley and Wilson (1), after reviewing the technique of BCG cultivation, point out that the virulence of BCG is continually falling and that the possibility exists that under such circumstances its protective value might disappear in time. It is important to recall in this connection the method of cultivation of BCG prescribed by Calmette (2). Briefly, it was recommended that BCG be cultured on a glycerinated potato slab in Roux tubes, the bottom portion of which contained 5 per cent glycerin at pH 7.0 to 7.2. At regular intervals the culture was returned to a similar tube containing a potato slab treated with ox-bile glycerin mixture and, in the bottom portion, 5 per cent glycerin in ox-bile. Calmette believed that the reduction in the virulence of BCG resulted from cultivation in the presence of ox-bile. Griffith (3) was able to show that a pathogenic bovine strain of the tubercle bacillus did lose virulence under such conditions of cultivation.

Holm (4), in discussing the use of BCG in Denmark, makes the statement that the culture kept at the State Serum Institute in Copenhagen is transferred only occasionally to a medium containing ox-bile and only then when it is apparent that BCG is "weakened in virulence." Moreover, he states "... a new increase in virulence was obtained by several passages on bile potato." It is difficult to understand this assertion in the light of Calmette's original thesis and of Griffith's (3) work. One would expect that the return to cultivation on bile-potato medium would act in a reverse fashion.

In the BCG laboratory of the Municipal Tuberculosis Sanitarium of Chicago, in addition to the culture used for routine vaccination purposes, a strain of the organism has been maintained continually on ox-bile-glycerin-potato medium. It has been conscientiously transferred at two week intervals from 1934 to the present. In order to determine whether this treatment resulted in a loss in immunogenic ability, an experiment was performed which is detailed below.

MATERIALS AND METHODS

The culture of BCG used in these experiments has been kept under rigorous control since its arrival in this country in 1934. It has been cultivated by the methods prescribed by Calmette (2) and transferred at two week intervals. Thousands of guinea pigs have been used to test its avirulence and at no time has any evidence been apparent that this strain can cause progressive tuberculosis in guinea pigs. Intraperitoneal inoculation of several milligrams of the organism into guinea pigs results in, at most, the appearance of tubercles in the omentum and occasional tubercles in the liver and spleen. These lesions are self-limiting and usually have disappeared within one year.

Two groups of tuberculin negative (1:10 Old Tuberculin), commercially obtained guinea

[1] From the Department of Microbiology and Public Health, Chicago Medical School and the Municipal Tuberculosis Sanitarium of Chicago.

pigs were vaccinated by the multiple puncture method. On each guinea pig two areas on the back immediately lateral to the midline were shaved and cleansed. On each area a large drop of suspension of the culture was placed and through it 45 separate and discrete punctures were made. One group, composed of 16 animals, was vaccinated with what is designated for the purpose of this report "regular" vaccine, *i.e.*, a suspension of BCG prepared in the usual way for vaccinating human beings. The other group, composed of 18 animals, was inoculated with a suspension prepared from the culture which has been

TABLE 1

Tuberculin reactions of guinea pigs vaccinated with BCG

"REGULAR" VACCINE				"BILE" VACCINE			
Guinea Pig Number	Date Vaccinated	Date tested	Result[1] in mm.	Result[1] in mm.	Date tested	Date vaccinated	Guinea Pig Numbers
2420	11-18-46	1-8-47	$8 \times 8^{tr}_{.}$	$6 \times 6^{+}_{.}$	1-8-47	11-18-46	2402
3449	"	"	$10 \times 10^{+}_{.}$	$8 \times 10^{tr}_{.}$	"	"	2428
2426	"	"	$12 \times 10^{tr}_{.}$	$10 \times 10^{+}_{.}$	"	"	3047
2437	"	"	$12 \times 10^{tr}_{.}$	$8 \times 12^{tr}_{.}$	"	"	2416
3353	"	"	$12 \times 12^{tr}_{.}$	$12 \times 12^{tr}_{.}$	"	"	3027
2494	"	"	$12 \times 12^{+}_{..}$	$12 \times 10^{+}_{.}$	"	"	3028
3281	"	"	$12 \times 12^{+}_{..}$	$12 \times 14^{tr}_{.}$	"	"	3041
2470	"	"	$12 \times 14^{+}_{..}$	$12 \times 14^{+}_{.}$	"	"	2491
2474	"	"	$10 \times 12^{++}_{..}$	$14 \times 12^{++}_{.}$	"	"	3040
2492	"	"	$14 \times 14^{+}_{..}$	$12 \times 10^{++}_{..}$	"	"	2408
3433	"	"	$14 \times 12^{++}_{..}$	$12 \times 12^{++}_{..}$	"	"	3039
3026	"	"	$14 \times 14^{++}_{..}$	$12 \times 12^{++}_{..}$	"	"	2455
3460	"	"	$14 \times 14^{+++}_{...}$	$14 \times 14^{+}_{..}$	"	"	2403
2443	"	"	$16 \times 14^{++}_{..}$	$18 \times 14^{+}_{.}$	"	"	2440
3051	"	"	$14 \times 16^{+++}_{..}$	$16 \times 12^{++}_{.}$	"	"	3260
3457	"	"	$18 \times 14^{+++}_{...}$	$16 \times 14^{++}_{..}$	"	"	2454
				$20 \times 14^{++}_{...}$	"	"	2430
				$16 \times 20^{+++}_{...}$	"	"	2446

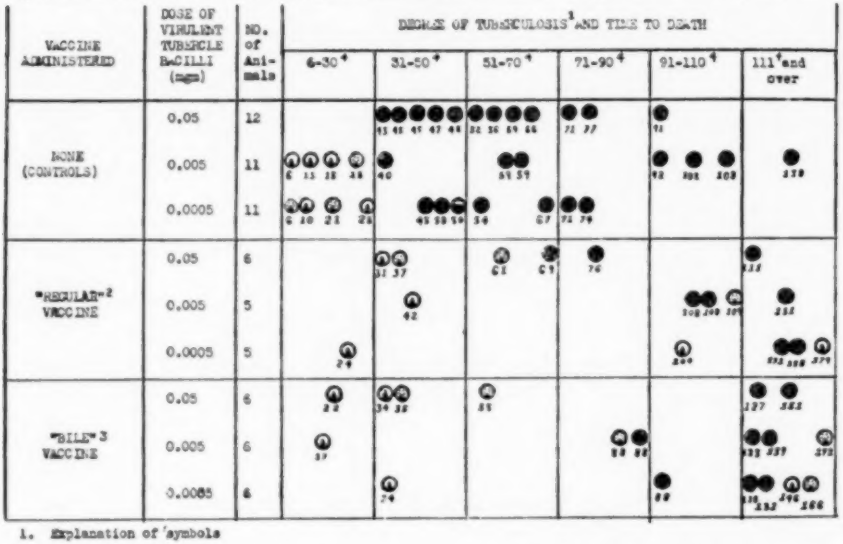
[1] The results of the test were read at forty-eight hours and measured in 2 diameters in millimeters. The degree of redness is indicated by the upper + sign and degree of edema by the lower. The latter takes into consideration the thickness of the edema. Tr. = trace. The reactions are arranged as closely as possible in increasing intensity by the National Tuberculosis Association standards. The 1+ reactions are on the first line, the 2+ reactions on the next twelve lines and the 3+ reactions on the last five lines.

kept continuously transferred in the ox-bile-glycerin-potato medium (the "bile" vaccine). Each vaccine was in a concentration of 15 mg. per cc.

Seven weeks after immunization, each of the guinea pigs was tested for tuberculin sensitivity by an intradermal injection of a 1:10 dilution of Old Tuberculin. One week later all the animals were injected subcutaneously with a suspension of a virulent tubercle bacillus (H_{37}). At the same time 34 normal tuberculin-negative guinea pigs, as controls, were injected with the same suspension and the same dosages of virulent tubercle bacilli. The viability of both the vaccine and H_{37} was controlled by inoculation of Löwenstein's medium at time of use. In each case viability was confirmed.

RESULTS

Following inoculation with BCG all the guinea pigs became positive to tuberculin. The results of the individual tests are noted in table 1. The reactions varied from 1 plus to 3 plus by the standards of the National Tuberculosis Association,[2] and examination reveals that, in the group vaccinated with the "bile" vaccine, 12, or 66.6 per cent, had 2 plus reactions and 5, or 27.7 per cent, had 3 plus reactions. In the group vaccinated with the "regular" vaccine, 12, or



1. Explanation of symbols

Generalized tuberculosis
Tuberculosis of liver and spleen
Occasional tubercles in liver and spleen
Local tuberculosis at point of inoculation only

Numbers under symbols indicate exact time to death in days

2. Vaccine prepared from culture regularly returned to ox-bile-glycerine potato medium after 5 transfers on plain glycerine potato.
3. Vaccine prepared from culture continously kept on ox-bile-glycerine potato medium.
4. Time to death in days after inoculation with virulent tubercle bacilli.

FIG. 1. The protective value of BCG in guinea pigs

75.0 per cent, had 2 plus reactions and 3 or 18.7 per cent had 3 plus reactions. This would seem to indicate that the degree of sensitivity induced by the "regular" vaccine was essentially the same as that induced by the "bile" vaccine. Under the conditions of this experiment, utilizing only a single test dose (10 mg. Old Tuberculin), it is impossible to affirm or deny that a difference in hypersensitivity exists between the two groups, as quantitative tuberculin testing was not done. In this experiment the tuberculin reaction was utilized only to prove the existence of infection engendered by the presence of BCG. For immunization purposes, a positive reaction to tuberculin, irrespective of degree, indicated a "take."

[1] + = an area of edema greater than 5 mm. but less than 10 mm.
++ = an area of edema greater than 10 mm. but less than 15 mm.
+++ = an area of edema greater than 15 mm.
++++ = necrosis irrespective of size.

In order to determine the degree of protection, the animals were divided into three secondary groups. Each group was given a different dose of the challenge tubercle bacillus (H_{37}), *i.e.*, 0.05 mg., 0.005 mg. and 0.0005 mg. In figure 1 are depicted the degree of tuberculosis and time to death of each of the various groups of guinea pigs. It is interesting to note that the three graded doses made remarkably little difference in the average time to death of the controls. Detailed examination of the figure makes it obvious that BCG, whether cultured intermittently or continuously on bile, confers a measurable degree of protection. This is further emphasized by the fact that 12 out of 16, or 75 per cent, of the animals vaccinated with either type of vaccine that finally died of generalized tuberculosis did so after 100 days. In the control group, only 3 out of 25, or 12 per cent, of the animals died more than 100 days after inoculation with H_{37}. In addition, there were 4 vaccinated guinea pigs that died of intercurrent infection 146 to 179 days after inoculation with virulent tubercle bacilli and showed little evidence of tuberculosis at autopsy.

By the same method of comparison it may be seen that 6 out of 8, or 75 per cent, of the animals immunized with the "regular" vaccine that finally died of generalized tuberculosis did so after 100 days. Exactly the same figures hold for the group vaccinated with the "bile" vaccine. Under the conditions of this experiment, there seems to be no significant difference between the immunogenic ability of the two types of vaccine.

SUMMARY

An experiment is described designed to determine whether the immunogenic ability of BCG, which is ordinarily cultured intermittently in the presence of ox-bile, is changed by continuous association with ox-bile. The results suggest that the possible loss of potency that could theoretically accrue to the vaccine because of exposure to bile has not yet made its appearance although BCG has been in continual cultivation on an artificial medium for thirty-nine years.

SUMARIO

Comparación de la Inmunogenicididad para el Cobayo del BCG Cultivado Intermitente y Continuamente en Presencia de Bilis

El experimento descrito se proponía determinar si la continua asociación con bilis de buey hace variar la capacidad inmunógena de BCG, que se suele cultivar intermitentemente en presencia de dicha bilis. El resultado denota que todavía no ha aparecido la pérdida de potencia que podria teóricamente aparecer en la vacuna debido a la exposición a la bilis, aunque BCG ha estado en cultivo continuo en medio artificial durante 39 años.

NOTE. Since the above article was submitted for publication, there has appeared the report of F. van Deinse (Am. Rev. Tuberc., 1948, *58*, 571) which confirms the experimental results reported here.

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AMERICAN TRUDEAU SOCIETY

Medical Section of the National Tuberculosis Association

STREPTOMYCIN IN THE TREATMENT OF TUBERCULOSIS

Report of Clinical Subcommittee

Committee on Medical Research and Therapy

Dr. John D. Steele, Chairman

Dr. Brian Blades
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Pulmonary Tuberculosis

Streptomycin has a limited but important place in the therapy of pulmonary tuberculosis. In general, streptomycin should be withheld if other satisfactory treatment is available.

Streptomycin therapy is not advisable in: (a) chronic fibroid or fibro-caseous pulmonary tuberculosis; (b) acute destructive and apparently terminal types of tuberculosis, except briefly and intermittently for purely symptomatic relief; (c) the minimal stages of pulmonary tuberculosis with a good prognosis, until attendant toxicity and incidence of resistant bacteria are more precisely defined.

Streptomycin appears to be most effective in the treatment of recent, acute, fairly extensive, and progressing pulmonary tuberculous lesions. Its use is particularly recommended in the treatment of tuberculous pneumonia.

Symptomatic relief and roentgenologic improvement are common in many types of pulmonary tuberculosis soon after initiating therapy with streptomycin. In general, the degree of benefit is in direct proportion to the extent of the acute or exudative component of the total disease being treated. As relapse is common, streptomycin is best used as an adjunct to other standard forms of treatment.

The following types of disease are regarded as especially suitable for streptomycin therapy: (a) acute bronchopneumonic tuberculosis with severe symptoms; (b) acute bronchogenic spread, particularly when of such a nature that much needed collapse therapy is prevented; and (c) chronic disseminated finely nodular tuberculosis without large confluent areas of destructive disease.

As streptomycin can only be used for periods of two to four months in the therapy of this chronic disease because of the emergence of resistant organisms, it is imperative that streptomycin be used for a period during the course of the disease when the greatest benefit can be expected.

The immediate benefits of streptomycin are usually limited to a period varying from several weeks to, at most, three months. Thus it is extremely important that the period of chemotherapy be worked into an over-all plan of treatment which frequently will include collapse therapy and generally includes institutional care.

The Committee looks with disfavor on the practice of utilizing streptomycin prior to institutional care or as an alternative to collapse therapy in the hope that such treatment might be avoided.

Ulcerating Tuberculous Lesions of Mucous Membranes

Ulcerating lesions of mucous membranes usually respond well to streptomycin therapy. Included in this group are laryngeal, tracheal, bronchial, oropharyngeal, and enteral ulcerations, and tuberculous otitis media, and streptomycin is recommended for these conditions.

Streptomycin is most effective in tuberculous lesions of the larynx and tracheobronchial tree which are ulcerating; somewhat less so but still effective in lesions which are granulomatous; and still less effective in diffuse inflammatory lesions. It appears to be ineffective in purely cicatricial lesions. Other routes of administration, topical, aerosol, oral, are not sufficiently effective to be recommended as alternatives to parenteral administration.

With parenteral administration healing of ulcerative lesions is prompt. Streptomycin therapy may safely be discontinued soon after healing by epithelialization has been observed to occur (restitution of normal mucosal pattern roentgenologically in the case of tuberculous enteritis). In cases with an ultimately poor prognosis because of associated extensive pulmonary tuberculosis, streptomycin may be used for short and intermittent periods of time for its palliative clinical effects in treatment of clinical complications.

Tuberculous Sinuses and Fistulae

Streptomycin is recommended in the treatment of draining tuberculous sinuses and fistulae and appears to be highly effective in closing the infected tracts, at least temporarily, in a majority of cases, regardless of the underlying tuberculous disease.

For more permanent results in most instances, however, streptomycin is merely an excellent adjunct to suitable surgery, superior results being obtained only with this combined treatment. Such surgical measures will include wide excision or incision and drainage, depending on the location and nature of the underlying tuberculous pathology and are best instituted prior to, or at the time of, institution of streptomycin therapy.

Genito-urinary Tract

Streptomycin is recommended in the treatment of tuberculosis of the genito-urinary tract. As a rule this will be in conjunction with other indicated therapy, especially surgery. Symptomatic relief and increase in bladder capacity are common, and the urine is sterilized in many, although only temporarily in some. Results are compromised by the fact that most clinically detected cases of renal tuberculosis are far advanced with caseation, and streptomycin is least effective in these cases.

Tuberculosis of Bone, Joint and Cartilage

Streptomycin is advised in the treatment of tuberculosis of bone, joint and cartilage, particularly in conjunction with other accepted forms of therapy. Because the effect of streptomycin therapy may be long delayed in becoming apparent, it is important to exercise discriminating judgment in the timing of the use of the drug as an adjunct to other procedures.

Tuberculous Meningitis

Intensive therapy with streptomycin, administered both parenterally and intrathecally, is imperative for the treatment of tuberculous meningitis. Intramuscular therapy should be continued for from four to six months. As indicated below, the recommended dosage for intramuscular administration is two grams a day. It is recommended that

not more than 50 mg. of streptomycin be administered intrathecally every second or third day for the greater part of the period of treatment, although this amount may be given daily for the first five to seven days.

Although neurologic complications arising as a result of this regimen are frequent and may be serious, complete clinical remission in an appreciable number of cases is observed. The response is best when diagnosis is early and treatment prompt so that bacteriologic confirmation need not be secured prior to institution of therapy.

To avoid the dangers inherent in treating a nontuberculous meningitis with streptomycin, it is wise not to institute therapy with streptomycin unless at least one of the following conditions is met: (a) an associated active tuberculous focus is present with a positive tuberculin test, or (b) cerebrospinal fluid cultures are negative for ordinary pathogens and the characteristics of the spinal fluid are in keeping with those of tuberculous meningitis.

Miliary Tuberculosis

Streptomycin therapy is indicated in the treatment of both acute hematogenous (miliary) tuberculosis and chronic hematogenous disseminated tuberculosis.

Good clinical judgment is needed to differentiate these conditions from nontuberculous pulmonary infiltrations simulating miliary tuberculosis, especially in the early stages. Despite this difficulty, early treatment is highly desirable and in appropriate instances should be started even before bacteriologic confirmation is obtained. Bone marrow biopsy and culture of material for acid-fast bacilli may be a useful aid in early diagnosis. Treatment should be continued for at least four months and one to two grams a day is adequate dosage.

Development of tuberculous meningitis is a common hazard in the course of acute miliary tuberculosis. It may occur during or shortly after therapy with streptomycin. Because the onset of this complication is frequently insidious, it is recommended that routine lumbar punctures be performed at intervals during the six to eight months after the diagnosis of miliary tuberculosis. Intrathecal therapy should be added whenever the cerebrospinal fluid is found abnormal before the advent of clinical evidences of central nervous system infection.

Tuberculous Lymphadenitis

Although there is some doubt as to whether streptomycin should be employed in the treatment of tuberculous lymphadenitis, as in the case of minimal pulmonary tuberculosis (see above), it may be employed in the treatment of lymphadenitis, especially in the acute stage. It is probable that the majority of such lesions treated with streptomycin will regress or disappear promptly, although relapse may occur.

Tuberculous Peritonitis and Pericarditis

Streptomycin is recommended in the treatment of tuberculous peritonitis, for clinical remission is common and relapse relatively infrequent following adequate therapy. Streptomycin may not be expected to alter the sequelae of tuberculous pericarditis but appears to have a beneficial effect on the acute process itself.

Skin and Ocular Tuberculosis

More extensive observations will be required to evaluate the effect of streptomycin in the therapy of tuberculosis of the skin and the eye.

Streptomycin and Surgical Procedures

Streptomycin appears to be beneficial when employed prophylactically for short periods of time in association with certain surgical procedures. This is particularly true for single-stage operations, where prolonged administration of streptomycin is not required. Employed for short periods before and after operation, streptomycin has markedly decreased the hazards of pulmonary resection for tuberculosis by diminishing the incidence of early postoperative spreads.

It is not considered advisable to employ streptomycin as a routine prophylactic in multiple-stage operations for tuberculosis.

Dosage and Duration of Streptomycin Therapy

Much remains to be determined as to the optimal dosage and duration of streptomycin therapy. It is probable that no single streptomycin regimen is suitable for all types and forms of tuberculosis. With smaller daily doses of streptomycin, there is relatively little danger of toxicity; but the problem of the emergence of drug-resistant strains of organisms remains unsolved.

One gram a day may be sufficient for the majority of tuberculous lesions, with the exception of tuberculous meningitis and miliary tuberculosis, where more may be advisable (see above). There is some evidence that some regimens of two grams a day produce better therapeutic results. The higher incidence of toxic manifestations on the regimens using the larger dosages must be balanced against their possibly greater efficacy.

Frequency of administration need not be greater than every twelve hours. It is advised that streptomycin therapy be administered in courses of forty-two days (which may be repeated, if necessary) to reduce the incidence of emergence of drug-resistant organisms. This recommendation does not apply in the case of miliary tuberculosis and tuberculous meningitis, where, as noted above, it is recommended that treatment be continued for at least four months.

In individual cases it may be necessary to weigh the therapeutic advantages that might accrue from longer periods of treatment against the disadvantage of the emergence of drug-resistance. Until further studies have been concluded, it cannot be recommended that injections be made less frequently or that treatment be continued for shorter periods of time than here indicated.

Toxic Manifestations of Streptomycin Therapy

Toxic manifestations are relatively infrequent on the dose recommended above, *i.e.*, one gram a day. Nevertheless the following reactions do occur and whenever treatment with streptomycin is contemplated, the dangers of the untoward side reactions should be compared with the hazards of the tuberculous disease being treated:

(a) A disturbance of vestibular function may be observed, especially following prolonged treatment with larger doses. Partial or complete compensation is frequently noted, especially in younger persons, but the potentialities of this disorder must not be underestimated by the physician. It has not been determined if this disadvantage to streptomycin therapy can be overcome.

(b) Deafness may be produced in very rare instances and only following larger doses or when streptomycin excretion is defective. Useful hearing is nearly always regained if treatment is suspended promptly when deafness is noted. Audiometric observations are probably advisable at this time until the conditions under which deafness occurs are better defined.

(c) Serious renal damage produced by streptomycin appears to be observed rarely except when there is pre-existing renal disease.
(d) Cutaneous rashes, apparently due to acquired hypersensitivity to streptomycin, are occasionally observed and sometimes indicate that treatment should be suspended temporarily. It is usually possible to resume treatment later. Serious exfoliative dermatitis is observed rarely.

Emergence to Predominance of Drug-resistant Tubercle Bacilli

The disappearance of drug-sensitive strains of tubercle bacilli and their replacement with strains which are drug-resistant present a serious handicap to prolonged effective therapy with streptomycin. It is not yet known what conditions encourage the appearance of drug-resistant organisms, how to determine drug-resistance with absolute precision, or how permanent this change in bacterial flora may prove to be. There appears to be a fairly uniform rate of appearance of such drug-resistance, related to the duration of treatment but independent of the daily dosage. The advantage of the forty-two day duration of therapy suggested is the probable avoidance of the emergence of drug-resistant strains in a larger percentage of cases. Retreatment is possible and feasible if the organisms remain drug-sensitive and the disease continues an unfavorable course or relapse occurs. Organisms should be tested for sensitivity before retreatment is undertaken, whenever practicable.

Dihydrostreptomycin

The Committee has reviewed limited experimental and clinical evidence concerning dihydrostreptomycin, a hydrogenated derivative of streptomycin. In most respects, the pharmacological properties of this compound, including absorption and excretion, are similar to those of the parent substance and in comparable doses dihydrostreptomycin and streptomycin apparently produce the same suppressive action on the tubercle bacillus, *in vitro* and *in vivo*.

The chief advantage of dihydrostreptomycin is that it is less toxic than streptomycin, especially in its action on the vestibular apparatus, when given in comparable doses for similar periods.

Despite the lowered incidence of toxicity, it should be pointed out that dihydrostreptomycin is not devoid of toxic potentialities. In addition to neurotoxicity, abdominal discomfort, nausea, vomiting, and skin rashes have occurred in a few instances. Another possible advantage of this compound is that it appears to be well tolerated by some patients who have developed hypersensitivity reactions to streptomycin. These advantages seem promising and warrant extensive clinical trials.

Some preparations of dihydrostreptomycin have produced local irritation at the site of injection; such preparations should not be used intrathecally. Unfortunately, strains of tubercle bacilli resistant to dihydrostreptomycin emerge in the same manner as to streptomycin, and organisms resistant to one compound are equally resistant to the other.

AMERICAN TRUDEAU SOCIETY

Postgraduate Courses in Pulmonary Diseases

The following postgraduate courses in pulmonary diseases are scheduled for the first half of 1949 by the American Trudeau Society, Medical Section of the National Tuberculosis Association. This program is conducted under the auspices of eight regional committees, covering all states, and the provinces of Canada, in cooperation with the medical schools of leading universities.

Applications may be obtained from the American Trudeau Society, 1790 Broadway, New York 19, New York. These courses are generally oversubscribed and physicians interested in applying are urged to request application forms as early as possible.

By special arrangement with the Department of Medicine and Surgery of the Veterans Administration, physicians employed by that agency are invited to participate. The request for detail to these courses originates in the branch and regional offices of the Veterans Administration and duplicate applications are required.

Physicians applying under Public Law 346, (G I Bill) should so state when filing applications with the Society.

January 24–29, 1949 **Los Angeles, California**	**Region VII comprising the states of: Washington, Oregon, California, Idaho, and Nevada; and the provinces of Alberta and British Columbia, Canada. This one week course will be held in cooperation with the College of Medical Evangelists, the University of Southern California School of Medicine, and the University of California at Los Angeles Medical School.** **Tuition—$50.00**
March 7–12, 1949 **Indianapolis, Indiana**	**Region V comprising the states of: Ohio, Indiana, Michigan, Illinois, Wisconsin, Missouri, Iowa and Minnesota; and the provinces of Manitoba and Saskatchewan, Canada. This one week course will be held in cooperation with Indiana University School of Medicine.** **Tuition—$50.00**
March 13–26, 1949 **New Orleans, Louisiana**	**Region IV comprising the states of: Alabama, Arkansas, Louisiana, Missippi, Oklahoma and Texas. This two week course will be held in cooperation with Tulane University of Louisiana School of Medicine and Louisiana State University.** **Tuition—$100.00**
April 4–9, 1949 **Atlanta, Georgia**	**Region III comprising the states of: Maryland, Virginia, West Virginia, Kentucky, Tennessee, North Carolina, South Carolina, Georgia, Florida and the District of Columbia. This one week course will be held in cooperation with Emory University School of Medicine.** **Tuition—$50.00**
July–August, 1949 **Denver, Colorado**	**Region VI comprising the states of: Colorado, North Dakota, South Dakota, Nebraska, Kansas, New Mexico, Arizona, Utah, Wyoming and Montana. This two week course will be held in cooperation with the University of Colorado School of Medicine.** **Tuition—$100.00**

Spring or Summer, 1949	Region VIII is planning a course at Saranac Lake, N. Y., chiefly for physicians from Northern New York and the Canadian Province of Quebec. This will be held in cooperation with medical schools of the area and The Trudeau Sanatorium. The dates have not yet been announced but information will be sent to those requesting it when available.

Special attention is directed to the following course for general practitioners which is being given in cooperation with The St. Louis University School of Medicine, January 17, 18, 19, 1949. Applications for this course should be obtained from the Executive Secretary of the Missouri Trudeau Society, 411 North 10th Street, Room 505, St. Louis 1, Missouri.

This is the second course for general practitioners included in the American Trudeau Society's program of postgraduate opportunities. There follows a summary of some of the subjects to be presented by leaders in the field of pulmonary disease:

Symptomatology in Chronic Pulmonary Disease—Practical evaluation of cough, pain, hemoptysis and dyspnea. Julius L. Wilson, M.D., Professor of Clinical Medicine, Tulane University School of Medicine; Head of Section on Chest Diseases, Ochsner Clinic, New Orleans, La.

Physical Examination of the Chest—its limitations. Paul Murphy, M.D., Assistant Professor of Clinical Medicine, St. Louis University School of Medicine, St. Louis, Mo.

Chest Films—how to obtain satisfactory ones. Don C. Weir, M.D., Senior Instructor in Radiology, St. Louis University School of Medicine, St. Louis, Mo.

Skin Tests—their importance in the diagnosis of lung diseases. Herbert L. Mantz, M.D., Tuberculosis Controller, Kansas City, Mo., Consultant in Tuberculosis, Veterans Administration.

The Five Cardinal Points in the Diagnosis of Clinical Pulmonary Tuberculosis. George D. Kettelkamp, M.D., Medical Director, Robert Koch Hospital; Assistant Professor of Clinical Medicine, Washington University School of Medicine, St. Louis, Mo.

Basic Concepts and Objectives in the Treatment of Pulmonary Tuberculosis. Carl Muschenheim, M.D., Associate Professor of Clinical Medicine, Cornell University Medical College, New York, N. Y. (Dr. Muschenheim also will speak on "Streptomycin in the Treatment of Tuberculosis.")

Among other subjects to be presented are: extra pulmonary tuberculosis, special problems in the management of tuberculosis such as pregnancy, diabetes, syphilis, surgical operations; tuberculous pleurisy with effusion, its management from the standpoint of avoiding subsequent phthisis; public health aspects of pulmonary tuberculosis, mass X-ray surgery, tuberculin testing, general hygiene; the pneumonias, practical points in the diagnosis and management; bronchiectasis; empyema thoracis; bronchogenic carcinoma; mediastinal tumors; mycotic diseases of the lung; the pneumoconioses; use of oxygen therapy, and rare diseases of the lung.

THE

AMERICAN REVIEW OF TUBERCULOSIS ABSTRACTS

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Streptomycin for Tuberculous Meningitis.—Clinical trials of streptomycin in the treatment of tuberculous meningitis in Great Britain were conducted under the supervision of a committee of the Medical Research Council. The results in 105 cases are reported. Of these, 71 have died, 33 are making good progress and one is deteriorating after seven or more months of treatment and observation. The prognosis in children under 3 years of age was much worse than in older children. The prognosis was better in the early stages of the disease than in the later. The results in patients who received only intramuscular streptomycin were much poorer than in those receiving the drug both intramuscularly and intrathecally. Nevertheless, it was felt that daily intrathecal treatment sustained over a long period ceases to be beneficial and probably is harmful. It was felt also that periods of complete rest from streptomycin treatment are beneficial. The streptomycin levels in the cerebrospinal fluid were found to be lower in patients who were recovering than in those who were deteriorating. Among the fatal cases 4 types were noted: (*1*) no response to treatment, (*2*) slow progressive deterioration with no period of improvement, (*3*) progressive deterioration after a short initial period of improvement or no change, and (*4*) relapse after a long period of improvement. In all but the first group, life was prolonged far beyond the normally expected period. As a result of the longer period of survival, spinal block and hydrocephalus were found in greater frequency than heretofore. In patients who ultimately fared badly, tubercle bacilli were isolated from the cerebrospinal fluid much more frequently during the first three weeks in patients who did poorly than in those who made good progress. Strains isolated from 22 patients treated up to 136 days were found resistant to streptomycin in only 3 cases.—*Streptomycin Treatment of Tuberculous Meningitis, Medical Research Council, Lancet, April 17, 1948, 1: 582.*—(*A. G. Cohen*)

Streptomycin for Tuberculous Meningitis.—A total of 18 cases of tuberculous meningitis were treated with streptomycin. Of these, 7 died and 11 survived; 4 of the latter are still under treatment. In most cases, the drug was administered both intramuscularly and intrathecally for at least six weeks and thereafter intramuscularly alone for the next four to six months. The average intramuscular dose was 2 Gm. daily for adults and 0.02 Gm. per lb. of body weight for infants, at first by divided doses and then by a single daily dose. After about four months, if the patient was doing well, a single injection of 2 Gm. was given every two days. The daily intrathecal dose was 0.1 Gm. for adults and 0.05 to 0.07 Gm. for infants, given as a single injection. When very strict antiseptic precautions were used, very few side effects were seen, except involvement of the eighth cranial nerve and gastric upsets. In the fatal cases, necropsy revealed extensive exudative changes in the meninges. These resulted in hydrocephalus, symptoms of cerebral anoxia or infection, and manifestations of hypothalamic disturbance. The diagnosis of ad-

vanced cases was relatively simple; it was easy to find acid-fast bacilli on smears and to confirm their pathogenicity by culture. In early cases, the diagnosis sometimes could not be proved immediately and treatment was begun in some cases before the organisms were identified. In all but 2 cases, frontal burr holes were made to provide access to the anterior horns of the lateral ventricles. If 7 to 10 ml. of fluid were obtained from each side, the diagnosis of brain abscess could be excluded and treatment begun earlier. Sometimes the organism was found more readily in the ventricular specimen than in the lumbar. Direct access to the ventricles for administration of streptomycin was thus provided. The object of treatment was to obtain as soon as possible a high level of streptomycin in the cerebrospinal fluid and to maintain this level. In the 7 survivors who have stopped treatment, neurological recovery is complete except for the eighth nerve.—*Treatment of Tuberculous Meningitis with Streptomycin, H. V. Smith, R. L. Vollum and H. Cairns, Lancet, April 24, 1948, 1: 627.*—(*A. G. Cohen*)

Streptomycin for Tuberculous Meningitis.—About 75 cases of spontaneous recovery from tuberculous meningitis have been reported in the literature. No case has ever recovered, however, in the past thirty-two years at the Boston City Hospital; the deaths have totalled 178. A 7-year-old boy has been treated with streptomycin and is clinically cured after one year. He received a total of 70,458,332 units intramuscularly and 2,675,000 intrathecally over a period of 141 days. He has several residual paralyses. Two other patients died after brief treatment; a third infant recovered clinically, was sent home with serious cerebral damage, and died thirteen months after the start of therapy; a fourth child, apparently completely well, died suddenly nine months after she was first seen, and a cerebral thrombosis and infarction (produced by the growth of a tuberculoma) were found, as well as miliary tubercles containing acid-fast bacilli. Early and intensive therapy is recommended.—*Tuberculous Meningitis Treated With Streptomycin, O. S. Nau, Jr. & F. J. Wenzler, J. Pediat., April, 1948, 32: 410.* (*W. H. Oatway, Jr.*)

p-Aminosalicylic Acid for Tuberculosis.—Five patients with pulmonary tuberculosis were treated with p-Aminosalicylic Acid for sixty days and one patient for four weeks. A total of 12 Gm. daily was administered in divided doses every three hours. Within a few days there was great improvement in the patient's general condition. There was a decline in fever and a decrease in the number of organisms. A blood level of 2 to 5 mg. per cent was reached with the stated dose. There were no toxic reactions. The author believes that the dosage and length of treatment were insufficient but that the drug is of value in exudative and toxic forms of tuberculosis.—*Pulmonary Tuberculosis Treated with p-Aminosalicylic Acid. A. Erdei, Lancet, May 22, 1948, 2: 791.*—(*A. G. Cohen*)

Whooping-cough and Tuberculosis.—In the ten years before August 1947, 1,747 patients were admitted to the Cleveland City Hospital with pertussis. All such patients routinely are tuberculin skin-tested, since the pulmonary symptoms of tuberculosis may be the same as those of pertussis and the findings by X-ray may be similar for several infections. In 38 patients the chest X-ray showed suspicious evidence of tuberculosis; in 23 patients the tuberculin test was positive; 19 actually had either primary, active, or arrested tuberculosis. Except in one case there was no evidence that tuberculosis was activated by pertussis. All patients ill with whooping-cough should have a tuberculin skin test to aid differential diagnosis.—*Does Pertussis Activate Tuberculosis?, J. A. Toomey, J. C. Berno, & H. Agustsson, J. Pediat., March, 1948, 32: 260.*—(*W. H. Oatway, Jr.*)

Coexisting Coccidioidomycosis and Tuberculosis.—Only 3 such cases are recorded in the literature. There have been recent verbal reports of several more. The authors report a case of cavitation due to coccidioido-

mycosis. After fifteen months, the patient developed cavitary tuberculosis in the opposite lung.—*Coexisting Pulmonary Coccidioidomycosis and Tuberculosis, R. S. Study & P. Morganstern, New England J. Med., June 10, 1948, 238: 837.*—(*A. G. Cohen*)

Serous Tuberculosis in African Negroes.—Among native African troops between the ages of 18 and 30, 169 cases of serous pleuritis were seen. These are divided as follows: primary glandular tuberculosis with effusion, 16, primary unilateral effusion, 125, and tuberculous polyserositis, 28 cases. The 16 cases of primary glandular tuberculosis with effusion are part of a group of 36 cases of primary glandular tuberculosis. The patients gave a history of fever, cough and slight expectoration for several weeks. Some showed no local signs or symptoms and were first regarded as cases of unexplained fever. Others showed signs of local consolidation and were first regarded as pneumonia. X-rays showed, besides the effusion, enlarged nodes and occasionally hilar flare or definite lobar or segmental collapse. Sputum and gastric studies were negative for tubercle bacilli. The effusion appeared at the onset in 7; in the other 9 it appeared after three to four months. The course in all patients was benign; there were no deaths. The temperature gradually fell and the fluid absorbed but the glandular enlargement persisted. The second group consists of 125 cases of primary pleural effusion with no deaths. The onset in some was subacute with chest pain, fever and dry cough. In others, the onset was insidious with general malaise and minimal local symptoms. In others, there was an acute onset with high fever and severe pleuritic pain; these cases were diagnosed as pneumonia at first. In 12 per cent, there was enlargement of the supra-clavicular, less often the cervical, lymph nodes. In the few cases checked, cultures of the fluid were negative. The cells were predominantly lymphocytes. The sputa were negative. The white blood counts were normal. The subsequent course was characterized by a fall in temperature and gain in weight. There was a gradual fall in sedimentation rate; higher final figures were found in cases with the most residual pleural thickening. It was impossible to enforce bed-rest after the initial acute stage. In about one half of the cases the fluid was allowed to absorb without interference; in the other half, it was aspirated as indicated. The final results showed considerable pleural thickening in 70 per cent; there was little difference between the 2 groups. Criteria for arrest were: (*1*) normal temperature for three weeks, (*2*) absorption of fluid, (*3*) significant weight gain, and (*4*) progressive fall in sedimentation rate. This required about four to five months. The third group consists of 28 cases of polyserositis. These are divided as follows: (*1*) presenting as primary glandular tuberculosis, with subsequent generalized miliary spread, 3 cases, all fatal; (*2*) primary serous tuberculosis, with subsequent consecutive effusions of the polyserositis type, 11 cases with one death; and (*3*) primary serous tuberculosis with subsequent polyserositis, 14 cases with one death. In these 28 cases, 20 presented as a unilateral pleural effusion; a contralateral effusion appeared within eighteen months in 15. Pericardial effusion was found in 8 and abdominal glandular and serous tuberculosis in 10 cases. Anatomically, all the cases were characterized by marked tracheobronchial lymph node tuberculosis. The disease then progressed from one chain of glands to the other and may have been the cause of the pleural effusion. Unlike the case in Europeans, primary pleural effusion in African Negroes is linked with slow continuous or intermittent evolution of primary tuberculosis. It appears in the post-primary stage within about six months and displays 3 tendencies unusual in European adults: (*1*) it is an incident in a predominantly glandular syndrome; (*2*) it may develop into polyserositis; and (*3*) at any point, miliary dissemination may supervene.—*Serous Tuberculosis in East African Natives, S. R. Wood, Brit. J. Tuberc., April, 1948, 42: 38.*—(*A. G. Cohen*)

Congenital Tuberculosis.—A previous definition of congenital tuberculosis has been "tuberculosis in which the infection occurs before birth by way of the blood stream or by aspiration of the amniotic fluid or contents of the birth canal." The authors agree with the first portion, but believe that those cases which result from aspiration in the birth canal should be called "tuberculosis neonatorum." Several reviews of the literature in recent years have "authenticated" 100 cases, more or less, and some believe that intra-uterine infection is quite rare. The authors report the case of a Negro infant, removed from its home within an hour after a normal birth, which died on the forty-fourth day of acute miliary tuberculosis, proved at necropsy. The mother died sixty seven days post partum of a "miliary tuberculosis," diagnosed by X-ray of the chest. She also had a positive Wassermann, a negative tuberculin skin test, and a foul vaginal discharge.—*Congenital Tuberculosis. A Review of the Disease With Report of a Case, E. A. Harris, G. C. McCullough, J. J. Stone, & W. M. Brock, J. Pediat., March, 1948, 32: 311.*—(*W. H. Oatway, Jr.*)

Extrapleural Pneumolysis with Lucite Plombage.—There has been a continuous search for the ideal substance to fill the extrapleural space in plombage. Certain experimental work suggested that methyl methacrylate, known commercially as lucite, was well suited for this purpose. Balls of this substance were used in operations on 30 cases. The lesions were of the same type as those for which thoracoplasty would ordinarily be performed except that those with large thin-walled cavities were not taken. Lesions down to the third anterior rib were considered operable. Advanced age and bilaterality were not considered contraindications. All were pneumothorax failures. An average of 20 to 35 lucite balls were used in each operation. The postoperative course generally was uneventful. All patients developed fluid in the extrapleural space. The febrile reaction was mild. Subcutaneous emphysema was infrequent. The pleura was torn in 3 cases but with no serious outcome. Most patients had some pain. The advantages of the operation are lack of deformity, absence of paradoxical motion and less loss of pulmonary function. An economic advantage is the fact that it is performed in one stage. It is a more difficult operation than thoracoplasty. The ultimate fate of the lucite is unknown.—*Extrapleural Pneumonolysis with Lucite Plomage, J. B. Grow & R. E. Dwork, Brit. J. Tuberc., April, 1948, 42: 24.*—(*A. G. Cohen*)

Extrapleural Pneumonolysis. — Lateral thoracid branches of the internal mammary artery occur in approximately 50 per cent of individuals. These vessels course over the inner aspect of the upper and anterolateral area of the chest wall. They may be damaged when giving refills after an extrapleural pneumonolysis, resulting in serious hemorrhage into the extrapleural space. Moderate or massive hemorrhage occurs in 5 to 20 per cent of cases and may result in collapse of the patient or, more remotely, delayed infection or gradual obliteration of the space. When discovered at operation, the vessels should be ligated or coagulated with diathermy and, in addition, refills should at first be given from the back.—*Hemorrhage after Extrapleural Pneumonolysis, W. P. Cleland, Thorax, June, 1948, 3: 127.*—(*A. G. Cohen*)

Bilateral Collapse Therapy.—In a group of thoracoplasty cases, 11.2 per cent received contralateral pneumothorax. These were divided into 3 groups according to the postoperative results. Group A, comprising those with negative sputum, totaled 14 cases or 48.25 per cent. In all cases the lesions were arrested or quiescent. In group B, with positive sputum, there were 10 cases or 34.5 per cent. The lesions were stationary or improving in 5 and extending in 5. Group C contained 5 cases or 17.25 per cent; these were all dead. The initial prognosis in these cases, requiring thoracoplasty in the presence of an active contralateral lesion, is bad. The

pneumothorax must be managed with the greatest care. A marginal pneumothorax should be maintained and an attempt should be made to keep the lung at a constant distance from the chest wall. Three of 7 relapses and 2 of the 5 deaths resulted directly from premature abandonment of the pneumothorax. The optimum time for such abandonment is debatable. The author believes it should be maintained as long as possible.—*Bilateral Active Pulmonary Tuberculosis Treated with Artificial Pneumothorax and Thoracoplasty, G. P. Maher-Loughann, Tubercle, May, 1948, 29: 101.*—(*A. G. Cohen*)

Recurrent and Chronic Spontaneous Pneumothorax.—Seventy-one cases of recurrent and chronic spontaeous pneumothorax are reported. A case is considered chronic if the collapse lasts longer than three months. There were 46 such cases with an average duration of fifteen months. Of these, 29 were entirely chronic while in 17 chronicity supervened upon recurrent attacks. There were 25 purely recurrent cases; when combined with the 17 complicated by chronicity, they make a total of 42 recurrent cases. The average number of attacks was 4; the greatest number was 15. Chronic pneumothorax leads to invalidism and disability. In recurrent pneumothorax, the patient is doomed to a life of inactivity. It is believed that chronic and recurrent pneumothorax are manifestations of one aspect of the natural history of many lung diseases. The number of males greatly exceeded females. All decades of life were represented. There was a higher incidence in older decades than in pneumothorax simplex. Clinically, there was a greater coincidence of chronic bronchitis and emphysema. The condition often was noted accidentally. In chronic pneumothorax the loss of weight was striking. Plain radiographs may show nothing more than the pneumothorax. The first consideration is to decide whether it is actually a pneumothorax or rather a giant cyst or bulla. Diagnostic puncture is dangerous as it may lead to a severe pneumothorax; it should be done only when one is prepared to proceed with thoracotomy. The plain film should be inspected for evidence of cysts or bullae. These are easier to detect by tomography. Bronchograms occasionally are desirable; they may disclose unsuspected or asymptomatic bronchiectasis and may also help in differentiating between pneumothorax and cyst. Bronchoscopy occasionally is helpful. Pleural pressure readings which quickly revert to the original after aspiration are diagnostic of a bronchopleural fistula. Determination of the carbon dioxide, oxygen and nitrogen content of the pleural air also may help to determine the presence of a fistula. The most valuable diagnostic procedure is thoracoscopy. The following types of underlying lesion were found: generalized emphysema in 12, bullous emphysema in 13, asthma and bronchitis with emphysema in 8, large solitary bullae or cystic disease in 11, diffuse polycystic disease in 3, small bullae, mostly apical, in 15, apical scars in 6, leak or tear seen in 4, areas of "cuckoo-spit" in 4, various, such as tooth extraction, staphylococcus abscess, drainage of empyema and tuberculous pleurisy each in one and no cause in 6. "Cuckoo-spit" is a name given to a condition in which there is an ooze of air bubbles from an apparently normal lung surface. Thus, the cause of spontaneous pneumothorax may lie in a defect in either the pleura, subpleura, alveoli or bronchi. Large cysts or bullae are treated surgically by excision or lobectomy. In other cases, pleurodesis is effected. The author prefers to use silver nitrate. Four swabs of a 20 per cent solution are first applied directly to the lung surface at the time of thoracoscopy. Later, 5 to 10 minims of a 10 per cent solution are injected. This results in fever and effusion. There must then be judicious aspiration of air and fluid.—*Recurrent and Chronic Spontaneous Pneumothorax, R. C. Brock, Thorax, June, 1948, 3: 88.*—(*A. G. Cohen*)

Welder's Siderosis.—In 1936, shadows were discovered in the chest X-rays of electric-arc welders. These men were apparently in

good health. It was believed that the shadows probably were due to deposition of iron oxide. Fibrosis does not result from this. Since then, many electric-arc, carbon-arc and oxyacetylene welders have been examined and similar shadows were found in each group. In 1945, 15 of the original subjects were re-examined; all but 2 had continued at the same occupation. Of 7 whose X-rays had shown no abnormalities, one was suspicious and one showed definite changes. In 2 with suspicious shadows, the changes had become definite. Of 6 with positive findings, 4 were still so, one appeared to be clearing and one was negative. Siderosis is one of the benign pneumoconioses in which dusts deposited in the lungs give characteristic X-ray changes but no disability. These changes are not necessarily permanent.—*Clearing of X-ray Shadows in Welder's Siderosis, A. T. Doig & A. I. McLaughlin Lancet, May 22, 1948, 2: 789.*—(*A. G. Cohen*)

Bronchiectasis.—In a military hospital, 211 men and 3 women aged 18 to 49 showed symptoms and signs resembling chronic bronchitis. Bronchography was performed for all; 46 (21 per cent) showed bronchiectasis. There was a past history of pneumonia in 26; in 6 there had been 2 or more attacks and one patient had had 4 attacks. Pleurisy alone had been present in 3 cases. There was no evidence of tuberculosis although suptum examinations had been made for about half of the cases. Four patients had had measles and one had pertussis. The most frequent previous symptom was a winter cough. Currently, the patients suffered from productive cough and dyspnea. The cough was aggravated by changes of temperature and by smoking. In most cases, it was severe enough to cause disability. The sputum was either white mucoid or thick yellow and gave no odor; about 2 to 3 ounces were produced in twenty four hours. Night sweats were present in 7 cases, loss of weight in 2 and mild hemoptysis in 12. Examination showed diminished respiratory excursions in all cases. Clubbing of the fingers was found in 8 cases. Impairment of percussion note, poor air entry and coarse rales were common. The signs and symptoms were the same in both the bronchitis and bronchiectasis group, but were more frequent in the latter. The bronchiectases as demonstrated by bronchography were cylindrical in 31, varicose in 3 and saccular in 12. Plain chest films showed increased markings which were sometimes crowded together. More rarely there were localized zones of increased translucency in the middle or outer part of the lower lobe. This sign, if found, is very reliable. Other changes described in the literature are not definitive and bronchography is essential for diagnosis. The bronchi in unresolved pneumonia may first undergo reversible mechanical dilation which may later be rendered irreversible by infection. The reversible state lasts for several months.—*Bronchiectasis Simulating Chronic Bronchitis, J. D. H. Wearing, Lancet, May 29, 1948, 1: 822.*—(*A. G. Cohen*)

Liver Biopsy in Sarcoidosis.—Aspiration liver biopsies in 3 cases which presented clinical features suggesting a diagnosis of sarcoidosis showed typical noncaseating tubercles. In one case, serial sections were necessary. A typical lesion also was found in a liver biopsy from a patient presenting no other evidence of the disease.—*Liver Biopsy in Sarcoidosis, J. G. Scadding & S. Sherlock, Thorax, June, 1948, 3: 79.*—(*A. G. Cohen*)

Prophylaxis of U.R.I.—One hundred and forty-eight children, living in a metropolitan area and susceptible to various upper respiratory infections, were given 50,000 units of buffered penicillin in tablet form before two meals a day for one year. The effect was determined by comparing the number of infections and the days of fever with those of the previous year and against those of 110 comparable controls who received no penicillin. Cultures and blood levels were not determined. The controls showed no change in the incidence of infection or days of fever. The treated group showed a decrease in the

number of infections to 45.5 per cent of the previous year, and a decrease of febrile days to 25.3 per cent. This confirms the results of a previous test in which 25,000 units per day and influenza virus vaccine were used. Only three children showed any toxic reaction; there was no evidence of a resistant bacterial flora.—*Prophylaxis of Upper Respiratory Infections in Children Treated with Oral Penicillin, J. H. Lapin, J. Pediat., February, 1948, 32: 119.*—(*W. H. Oatway, Jr.*)

Spontaneous Pneumothorax.—One hundred consecutive cases of spontaneous pneumothorax were studied. Of these, 64 were known to have underlying pulmonary disease. In 20 per cent, there was a history of unusual exertion prior to the episode. In 80 per cent, it occurred during ordinary activity. Tuberculosis was noted in 38 cases, emphysema in 5, bronchiectasis in 5. Empyema, asthma, abscess, carcinoma, pneumonia and infarct each occurred in a few. The great majority of the patients were males; the average age was 27 years. In 3 patients, there were multiple recurrences; one other subsequently developed spontaneous mediastinal emphysema and another developed tuberculosis after 4 recurrences. Aspiration of air was necessary in only 3 cases; in the others bed-rest sufficed. In patients over 45 years of age, the appearance of spontaneous pneumothorax should arouse suspicion of underlying carcinoma.—*Spontaneous Pneumothorax, R. M. Myerson, New England J. Med., April 1, 1948, 238: 461.*—(*A. G. Cohen*)

Pneumonectomy.—One of the chief complications of pneumonectomy is infection of the site previously occupied by the lung which has been removed (the gap). Various methods of obliterating the gap, including thoracoplasty, have not been successful. In the case described, pneumoperitoneum was combined with Monaldi suction applied to the gap. The Monaldi phase must await closure of the bronchial fistula. With this method, the gap was obliterated in a few months.—*Closing the Pneumonectomy Gap, G. S. Eedy, Lancet, June 12, 1948, 1: 905.*—(*A. G. Cohen*)

Pulmonary Hydatid Disease.—The author reviews the treatment of 27 of his own cases of pulmonary hydatic cyst. The conservative type of operation is favored. If the lung is adherent to the chest wall and the cyst is not infected, the contents of the cyst are removed and the adventitia is drained. If the cyst is infected, the cyst space is drained following removal of the contents. If the lung is not adherent, then, in addition to the above, the adventitia is sutured to the chest wall and the pleural cavity is drained. Lobectomy may be necessary for (*1*) serious hemorrhage from the cyst space during a conservative operation; (*2*) residual bronchiectasis, if symptoms warrant it; (*3*) empty sac, if hemorrhage or infection warrant it; (*4*) an uncertain diagnosis; and (*5*) giant cyst. In the author's series, 23 patients were operated upon, with one death; 4 patients coughed up their cysts.—*The Treatment of Pulmonary Hydatid Disease, M. P. Susman, Thorax, June, 1948, 3: 71.*—(*A. G. Cohen*)

Aspiration of Timothy Grass.—Eight cases of aspiration of timothy grass heads were seen in patients ranging from 14 months to 14 years of age. A definite history of aspiration was obtained in 5 patients; all had shown immediate symptoms which were sustained and progressive. The early symptoms, fever, cough and weight loss, led to a variety of diagnoses. The possibility of foreign body was suspected in only 2 cases. Among late symptoms, there was intermittent fever despite chemotherapy. Foul sputum was found in 6 cases, massive hemoptysis in 2, and weight loss in 3. Clubbing of the fingers was not prominent. The chest X-rays, when finally made, were diagnosed as pneumonitis, atelectasis, pneumonia or abscess. Bronchiectasis was demonstrated by bronchography in 5 cases; in addition, multiple small abscesses were seen in one of these. Bronchoscopy was performed in 7 cases. The timothy head was recovered in 3 cases; it was not found in the other 4. In one case, complete recovery followed removal. The foreign body was retained from 2 to 36 months and

symptoms appeared 4 to 36 months prior to lobectomy in the others. The right lower lobe was resected in 6 cases and the left lower lobe in one. The postoperative course was uneventful in all but one case in which there was unexplained fever for several weeks. The patients have been well for two months to four years. There were no specific pathological changes due to timothy *per se*. Three basilar abscesses containing timothy were found. Of 4 cases of classical bronchiectasis, timothy heads were found in the ectatic bronchi in 2; the stem always pointed down and the barbules upwards. The most striking histological change was extensive connective tissue proliferation about the bronchi and vessels with extension along the pulmonary septa; this was most marked in the younger children. In the older children, localized abscess formation was more prominent.—*Bronchiectasis Following Aspiration of Timothy Grass, M. G. Carter & K. J. Welch, New England J. Med., June 10, 1948, 238: 832.*—(*A. G. Cohen*)

Mediastinal Bronchiogenic Cysts.—The vast majority of mediastinal cysts are congenital in origin. Those arising from the respiratory system are termed bronchiogenic; those from the digestive tract are called gastric or esophogeal cysts. There is no sharp line of distinction. The current discussion excludes intrapulmonary cysts. The increasing use of chest X-rays has revealed more than the rare cases formerly seen, and it now can also be said that they are sometimes symptomatic. Symptoms usually begin in adult life, when the cyst has grown enough to produce pressure on adjacent structures. Eight cases are reported in this series, the literature is reviewed, and collected cases are analyzed. Bronchiogenic cysts may be classed as paratracheal, carinal, hilar, paraesophageal, or miscellaneous. In the absence of infection, symptoms depend on the size and location of the mass. Symptoms, differential diagnosis, occurrence, and treatment are discussed. Because of the congenital origin, one must bear in mind the possible presence of other anomalies. In the several reports during the past few years, a summary of surgical results has been difficult, due to incomplete diagnosis, incomplete excision, the use of aspiration, et cetera. A posterolateral transpleural approach is recommended and other surgical suggestions are given. Of the 8 patients reported, 7 had an uneventful recovery, while the eighth recovered after the effects of pericardial manipulation and a flare-up of hyperthyroidism had subsided. Surgical excision is usually recommended for the condition even though asymptomatic when first discovered.—*Bronchiogenic Cysts of the Mediastinum, H. C. Maier, Ann. Surg., March, 1948, 127: 476.*—(*W. H. Oatway, Jr.*)

Treatment of Empyema.—Twenty patients with empyema were treated by aspiration of the pus and instillation of either penicillin alone or with other agents. Six cases were caused by pneumococci, 9 by streptococci, one by staphylococci, and the others by miscellaneous organisms. In 8 cases, the pus had a putrid odor. Cures were obtained in 16, while 4 required surgical drainage. The average time of treatment was fourteen days, the number of aspirations 7.7 and the daily dose of penicillin 63,250 units. Systemic penicillin also was given. No chronic empyemas developed. Complete evacuation of the pleural fluid was done daily, followed by instillation of 100,000 units of penicillin plus 1 Gm. of streptomycin or 2 to 4 Gm. of a sulfonamide drug, depending upon the sensitivity of the bacteria. This was continued until the cultures were sterile, during which time the walls of the cavity were kept apart. The space was then obliterated as quickly as possible by aspiration of liquid and gas every other day, supplemented by penicillin instillation. Causes of failure were: (*1*) inability to evacuate the cavity because of thick pus, (*2*) nonsusceptible organism, (*3*) inability to maintain antibiotic fluid in the cavity (large bronchopleural fistula), (*4*) multiple loculi and (*5*) recurrence.—*The Treatment of Empyema With Topical and Systemic Penicillin and Other Antibacterial Agents, W. E. Burnett,*

G. P. Rosemond, J. H. Hall & H. T. Caswell, Surg., Gynecol. & Obstet., July, 1948, 87: 44.—(A. G. Cohen)

Calcification in the Lungs.—A review of the discovery, distribution, and occurrence of calcification in the lungs has been made. A series of 13 Chicago children is reported whose chest X-rays showed calcification and whose tuberculin skin tests were negative. They all appeared normal but 8 had chronic cough and frequent respiratory infections. Bronchoscopy showed a roughening of the mucosa in the main bronchi but bacteriologically negative secretions. Twelve were skin-tested with histoplasmin, and 6 were immediately positive.—*Nontuberculous Pulmonary Calcification, A. D. Biggs & R. G. Rigby, J. Pediat., April, 1948, 32: 393.—(W. H. Oatway, Jr.)*

Anomalous Left Middle Lobe.—Accessory lobes of the lungs are not uncommon, the azygos lobe being the most frequent. The retrocardiac lobe at the right base is demonstrated radiologically in 0.5 per cent to 8 per cent of chest X-rays. The lingula of the left lung is the homologue of the right middle lobe and a fissure separating the upper from an anomalous middle lobe on the left has been described. Sante found this occurred in one of 5,000 autopsies. Chest X-rays of 3 patients showed a fine line running from the left hilum toward the periphery at about the level of the posterior end of the eighth rib. The editor, incidentally, mentions 2 additional cases of his own that show this fine fissure on the left.—*The Anomalous Middle Lobe of the Left Lung, G. L. Hardman, Brit. J. Radiol., February 1948, 21: 70.—(B. Hyde)*

Resistance Breathing.—When dogs anesthetized with nembutal were made to breathe against an airway resistance of 20 cm. of water during either inspiration or expiration, significant degrees of pulmonary edema, congestion, and hemorrhage were observed upon sacrifice at six to eight hours or at the time of spontaneous death. Bilateral cervical vagotomy did not increase the tendency to lung edema under these circumstances. Pulmonary lesions after resistance breathing appear to depend upon multiple factors and cannot at present be accounted for in terms of simple direct effects of pressure upon the pulmonary tissues and vascular bed. An analysis of actual mechanisms awaits acquisition of additional factual data.—*Observations on the Effects on the Lungs of Respiratory Air Flow Resistance in Dogs with Special Reference to Vagotomy, S. Zinberg, G. Nudell, W. G. Kubicek, & M. B. Visscher, Am. Heart J., May, 1948, 35: 774.—(G. C. Leiner)*

Atelectasis in Tuberculosis.—The authors deal with the question of involvement of the peripheral bronchi in cases of so-called opaque lobe occurring during pneumothorax. In 26 necropsies on cases with tension cavities the major bronchi to the affected area were found to be involved specifically in 83 per cent of cases. The chief changes, however, were in the surrounding areas of bronchopneumonia and in the small peripheral bronchioles. The bronchioles at first were infiltrated with plasma cells and lymphocytes; the lumens were flattened and later entirely obliterated. The course of events is depicted diagrammatically. In a cavity with tuberculous bronchopneumonia, artificial pneumothorax may kink the draining bronchus which is diseased and structurally weakened. This may result in a tension cavity. This, in turn, causes alteration of the alignment of diseased bronchioles in the vicinity with early collapse and infection of the alveoli. This final picture is the so-called opaque lung or atelectasis.—*"Atelectasis" during Collapse Therapy for Pulmonary Tuberculosis, J. Cuthbert & M. N. Nagley, Tubercle, July, 1948, 29: 154.—(A. G. Cohen)*

Pulmonary Circulation.—Studies of cardiac output and pulmonary arterial pressure were performed using the venous catheter technique in 3 normal individuals and in 8 patients with various types of chronic pulmonary disease. Measurements were made at rest and during exercise on a stationary bicycle.

Two of the 3 normal subjects showed a decrease in the mean pressure in the pulmonary artery during exercise; all showed a marked drop in pulmonary vascular resistance and a minimal increase in the work of the right ventricle during exercise. Three of the patients with chronic pulmonary disease showed a significant elevation of pulmonary arterial pressure at rest, and in all 8 cases the mean pressure increased during exercise. There was either no change or an increase in the pulmonary vascular resistance during exercise, and the work of the right ventricle was invariably higher than in the normal subjects at a corresponding work level. The findings indicate that the expansibility of the pulmonary vascular bed during exercise is limited in patients with chronic pulmonary disease. Anoxia may contribute to the elevation of pulmonary arterial pressure during exercise in those patients whose arterial oxygen saturation falls. The physiological evidence upon which an estimate of disability must be based in patients with chronic pulmonary disease is extended by these studies of the pulmonary circulation during exercise. (Authors' summary.)—*Studies of the Pulmonary Circulation at Rest and during Exercise in Normal Individuals and in Patients with Chronic Pulmonary Disease, R. L. Riley, A. Himmelstein, H. L. Motley, H. M. Weiner & A. Cournand, Am. J. Physiol., February 1, 1948, 152: 372.—(G. C. Leiner)*

Pressure Breathing and Cardiac Output.—Three types of intermittent positive pressure breathing have been differentiated by the shape of the curve of the pressure in the mask and have been correlated with the changes in cardiac output observed in 33 experiments on 29 human subjects. The three types of pressure curves were as follows: type I, symmetrical with gradually increasing and decreasing slopes and expiratory and inspiratory times approximately the same, and the final expiratory pressure above the atmospheric level; type II, asymmetrical with the pressure rapidly increasing during inspiration and rapidly dropping during expiration, long inspiratory and short expiratory intervals, and the final expiratory pressure above the atmospheric level; and type III, asymmetrical with the pressure gradually increasing during inspiration and suddenly dropping early in expiration to the atmospheric level, the expiratory time equaling or exceeding the inspiratory. Cardiac output was decreased more or less in proportion to the increase in mean mask pressure with curves of the first and second types. There was no decrease in cardiac output with the third type of curve. The net filling pressure of the right ventricle decreased as the mask pressure rose and increased as the mask pressure fell with all types of curves. The mean net filling pressure of the right ventricle was calculated for complete respiratory cycles during intermittent pressure breathing and during ambient breathing. This mean pressure was reduced in cases where the cardiac output fell during intermittent pressure breathing. Conversely, when the cardiac output was increased, the mean net filling pressure rose. Interpreted in terms of variation in the stroke volume, these changes suggest that the deficit in cardiac output, which was incurred during the inspiratory phase, is compensated for under the expiratory phase. When the pressure drop is rapid in expiration so that the resulting intrapleural pressure is low and the right ventricular net filling pressure high, compensation is complete if the expiratory time is of sufficient duration. The expiratory time must equal or exceed the inspiratory time in order that the number of heart beats during expiration may equal or exceed the number during inspiration. With the third type of curve, the time and pressure relationships permit complete compensation and the mean right ventricular net filling pressure is not decreased. With the first and second types, compensation is incomplete because the mask pressure does not drop rapidly with the first type. The expiratory time is too short with the second. Intermittent positive pressure breathing should provide a mask pressure curve that shows: (*1*) a gradual increase in pressure during inspiration, (*2*) a subsequent rapid drop

in pressure, (*3*) a mean mask pressure during the expiratory period as near the atmospheric level as possible, and (*4*) an expiratory time equal to or exceeding the inspiratory time. Adequate ventilation can be provided with the above type of pressure breathing in man with a minimal disturbance to the circulation, and this type would seem most desirable physiologically for administering artificial respiration.—*Physiological Studies of the Effects of Intermittent Positive Pressure Breathing on Cardiac Output in Man, A. Cournand, H. L. Motley, L. Werko & D. W. Richards, Jr., Am. J. Physiol., January, 1948, 152: 162.*—(*G. C. Leiner*)

Alveolar Pressure.—Measurements of the alveolar pressure and the simultaneous rate of flow of respired air in 21 human subjects are presented. The data for each subject can be described by an equation of the form $P = K_1V + K_2V^2$, where P is the alveolar pressure and V is the volume rate of flow. The constants K_1 and K_2 differ for different individuals. In the average subject an alveolar pressure of 1.8 cm. of water is required to produce a flow of 500 cc. per second. (Authors' summary.)—*Measurement of Alveolar Pressure in Human Subjects, A. B. Otis & D. F. Proctor, Am. J. Physiol., January 1, 1948, 152: 106.*—(*G. C. Leiner*)

Myocardial Metastases from Bronchogenic Carcinoma.—The purpose of the article is to correlate the occurrence of arrhythmias and auricular involvement in an unselected series of 148 cases of bronchogenic carcinoma. Myocardial involvement was demonstrated in 17 cases. Of these, 11 showed arrhythmias, consisting of paroxysmal auricular fibrillation in 5, permanent auricular fibrillation in 2, permanent auricular flutter in 2, paroxysmal flutter and fibrillation in one and paroxysmal extrasystoles in one. There was no rheumatic history or postmortem evidence of rheumatic fever, hypertension or degenerative heart disease in any case. The average age was 54.7 years in cases with arrhythmia and 44.0 years in cases with regular rhythm. The primary lesion was in the left lung in 8 cases and in the right in 9. The left auricle was involved in 14 cases, the right auricle in 7, the left ventricle in 2 and the right ventricle in none. The histological type was squamous cell in 5 and oat-cell in 8; one each showed giant and spheroidal cell, oat and spheroidal cell and undifferentiated carcinoma. Serial sections of the coronary arteries were not made so that it cannot be stated for certain that arteriosclerosis was not a factor in producing the arrhythmia in some cases. It is assumed, however, that malignant invasion of the myocardium was at least the major factor. In 358 cases of nonbronchial carcinoma, metastases to the myocardium were found in 19 cases. The lesion was primary in many organs but malignant melanoma and some sarcomas showed a particularly high incidence. None arose from the gastro-intestinal tract below the esophagus. Only one showed an arrhythmia. Thus, the incidence of myocardial metastases from bronchogenic carcinoma is greater than that from all other sources combined.—*Myocardial Metastases from Bronchial Carcinoma and Other Neoplasms, J. E. G. Pearson, Brit. J. Tuberc., April, 1948, 42: 81.*—(*A. G. Cohen*)

Action of Diaphragm in Emphysema.—The range of the diaphragmatic movements was examined under costal and abdominal pressure in 9 normal and in 34 emphysematous subjects. Costal pressure enabled the normal, but not the emphysematous subject, to lower the diaphragm more on maximum inspiration. Abdominal pressure enabled both groups to push the diaphragm higher up in maximum expiration; during quiet breathing it restricted the diaphragmatic movements to a minimum. In no cases did improvement of the vital capacity occur. Under costal pressure the vital capacity was always considerably reduced. Its reduction under abdominal pressure was much smaller. Nevertheless, patients who used belts for several weeks were found to have an increased vital capacity after the belts were removed. This improvement is due to the additional respiratory training

which the compression produced.—*The Influence of Costal and Abdominal Pressure on the Action of the Diaphragm in Normal and Emphysematous Subjects, H. Herxheimer, Thorax, June, 1948, 3: 122.*—(*A. G. Cohen*)

Electrocardiogram in Pneumothorax.—Electrocardiographic studies were made before and after induction of a therapeutic pneumothorax. Ten patients with right pneumothorax and 13 patients with left pneumothorax were examined. P-wave changes were not consistent in left pneumothorax; in right pneumothorax P_1 showed a tendency towards decrease in amplitude, P_3 showed a tendency towards increase. P-R intervals remained unchanged. In right pneumothorax, there was a tendency toward decrease of QRS in lead 1. There was a tendency toward a shift of the axis to the right, more so in right pneumothorax than in left pneumothorax. T_1 became smaller in right and left pneumothorax. T_3 became larger in 10 of 13 cases of left pneumothorax; in right pneumothorax, T_3 showed no consistent change. In right pneumothorax, there were no important changes of the QRS complexes in the precordial leads. In all cases of left pneumothorax, the QRS complexes became smaller in two or more precordial leads; in 11 of the 13 cases the QRS complexes became more inverted in two or more precordial leads. In right pneumothorax there were no consistent precordial T-wave changes. In all cases of left pneumothorax the T-waves became smaller or inverted in two or more precordial leads. After resorption of the pneumothorax air the electrocardiographic changes disappeared. There was no correlation of the electrocardiographic changes with the degree of cardiac displacement or with the presence or absence of adhesions.—*Electrocardiographic Changes in Pulmonary Collapse Therapy. I. Artificial Pneumothorax, D. Feldman & C. Silverberg, Am. Heart J., May, 1948, 35: 800.*—(*G. C. Leiner*)

Venous Pressure in Tuberculosis.—Abnormal venous pressures have been observed frequently in cases of thoracoplasty, intrapleural and extrapleural pneumothorax. Measurements of the peripheral venous pressure of 55 patients with pulmonary tuberculosis confirm earlier reports that pressure changes are inconstant, often transient, and usually present only on the side of the more extensive disease or of the collapse. Among the patients were 30 who were dyspneic at rest but in whom clinical and roentgenographic evidence of right heart failure was absent or questionable. In such patients, venous pressure determinations offer valuable help in detecting early right heart failure. Collapse therapy does not interfere because it produces a unilateral increase in the venous pressure. The presence of the hepatojugular reflux phenomenon of Pasteur and Rondot is further evidence of heart failure; it is not produced by collapse therapy.—*The Relationship of Peripheral Venous Pressures to Pulmonary Tuberculosis, A. Paley & M. M. Alexander, A. J. M. Sc., February, 1948, 215: 189.*—(*G. F. Mitchell*)

Pneumopericardium from Pneumothorax.—In 2 cases receiving artificial pneumothorax for pulmonary tuberculosis, pneumopericardium appeared. The pneumothorax was on the right in one and on the left in the other. The pneumopericardium rapidly absorbed following abandonment of the pneumothorax. It is felt that the underlying mechanism is a congenital pleuropericardial defect.—*Pneumopericardium Complicating Pneumothorax Therapy, P. Ellman & K. K. Hussain, Thorax, September, 1948, 3: 129.*—(*A. G. Cohen*)

Prognosis of Cavitary Tuberculosis.—Positive sputum is regarded as the criterion of the presence of a cavity. The fate, after 20 years, of 1,233 unselected patients with positive sputum was investigated. There was found to have been improvement in the number of patients surviving three and five years from 1934, 1935 and 1936 onward. There was also improvement in the eight year survival period during 1937 to 1939. This

improvement was due to the various advances in treatment and care that have taken place. There was insignificant improvement in the ten year survival period. These studies indicate that the greatest care must be used in evaluating the apparent efficacy of any new type of treatment.—*The Fate of the Tuberculous Cavity, B. Mann, Tubercle, June, 1948, 29: 131.*—(*A. G. Cohen*)

Therapeutic Pneumoperitoneum.—Seventy-four patients with pulmonary tuberculosis were treated by phrenic crush supplemented by pneumoperitoneum. The treatment was used in cases falling into several categories. As a supplement to a partially effective pneumothorax, it was successful in 3 and partly successful in one of 8 cases. The good results were obtained chiefly with basal or mid-zonal cavities. As the sole definitive measure, it was successful in 14 and partly successful in 4 of 35 cases. The good results were obtained chiefly with exudative disease, infiltrations without cavitation, and cavities with no significant fibrosis. As a preparation for major surgical procedures, both on the homolateral and contralateral sides, it was effective in accomplishing the limited objective in 16 of 19 and 5 of 8 cases, respectively. It failed in all 4 cases of far advanced disease. The chief complications were effusion in 4 cases, including one of fatal peritonitis, and a non-fatal air embolism in one case. The patients experienced very little discomfort. The pneumoperitoneum was maintained as long as pneumothorax would have been in the same case.—*Pneumoperitoneum: Its Place in Treatment, R. J. Keers, Brit. J. Tuberc., July, 1948, 42: 58.*—(*A. G. Cohen*)

Absorption of Pneumoperitoneum.—The rate of absorption of pneumoperitoneum was studied in 33 cases of pulmonary tuberculosis. The pneumoperitonea were classified arbitrarily as full, moderate and shallow. The average time required for absorption was eight weeks in the full, five and a half weeks in the moderate and two and a half weeks in the shallow. The rate of absorption of air was not affected by exercise, duration of the pneumoperitoneum or the presence of fluid. Ex-vacuo effusions did not develop.—*The Absorption of Pneumoperitoneum, W. Fox, Thorax, September, 1948, 3: 141.*—(*A. G. Cohen*)

Extrapleural Pneumothorax.—Extrapleural pneumothorax was employed in 128 patients with pulmonary tuberculosis. All but 5 patients were followed for at least five years or until death. Fifty-six (44 per cent) were dead, 58 (45 per cent) were alive and well while 14 (11 per cent) were alive but with symptoms. In 28 cases the extrapleural pneumothorax was used with an intrapleural pneumothorax on the same side ("combined" operation). In the other 100 cases, the extrapleural operation alone was done ("standard" operation). The mortality was 14 per cent in the "standard" and 21 per cent in the "combined" group. Tuberculous infection of the extrapleural space was detected in 13 per cent of the "standard" and 28 per cent of the "combined" group. Other frequent complications were nontuberculous infection of the space, bronchopleural fistula, hemorrhage, atelectasis and effusion. Very few late complications were seen in cases where a satisfactory pneumothorax had been obtained. In 27 of the 33 cases in which the pneumothorax was voluntarily abandoned after an average period of five years, there were no relapses or complications. Factors leading to a successful outcome of the operation were (*1*) a short period of symptoms, (*2*) a small cavity which was not obviously subpleural, and (*3*) minimal disease in the contralateral lung.—*Extrapleural Pneumothorax, A. T. M. Roberts, Thorax, September, 1948, 3: 166.*—(*A. G. Cohen*)

Open Intrapleural Pneumonolysis—In 13 cases of pulmonary tuberculosis receiving pneumothorax, adhesions were severed by an open operation. In each case, a closed pneumonolysis had been attempted previously. The advantages of salvaging an ineffective pneumothorax are obvious. The disadvan-

tages of this procedure are: (*1*) the operator may not be able to cut all the adhesions, and (*2*) the operation carries with it all the complications of pneumothorax, thoracoscopy and thoracotomy combined. The chief complications are pleural infection and breakdown of the suture line. Early results in this series were excellent improvement in 7 cases, good progress in 2 and no change in one. One patient is worse and 2 have died; in these 3, there was a complicating empyema.—*Open Intrapleural Pneumonolysis in the Treatment of Pulmonary Tuberculosis, R. A. Smith, Brit. J. Tuberc., July, 1948, 42: 51.*—(*A. G. Cohen*)

Tuberculous Lesions of the Spine.—Tuberculosis of the spine is primarily a destructive disease with little signs of bone repair in the early stages but it may be sclerotic. The intervertebral space is often preserved in spite of extensive destruction of several vertebral bodies. Later, narrowing of the intervertebral space may result from extrusion of the nucleus pulposus into the softened bony or ligamentous tissue. In contrast, other infections often cause early and complete destruction of the vertebral discs. Infections limited to the neural arches are practically always nontuberculous. The spread in tuberculosis occurs by extension under the anterior longitudinal ligaments with surface invasion of the vertebral bodies anteriorly. In contrast, other infections spread by direct extension from vertebral body to adjacent body through the intervertebral disc. The classical description of bone tuberculosis is that of bone destruction without sclerosis and with minimal new bone formation. During recent years, however, reports of tuberculosis of the spine have emphasized sclerosis as a conspicuous feature, even in the absence of secondary infection. The lesions may be very extensive and in one case there were tuberculous lesions in all stages of development in at least 8 vertebral bodies.—*Multiple Tuberculous Lesions Of The Spine, J. L. Feuchtwanger, Brit. J. Radiol., August, 1948, 21: 400.*—(*B. Hyde*)

New Mycobacterial Infection in Man.—The author reports 6 patients with cutaneous ulcers in which strongly acid-fast bacilli were demonstrated by biopsy. The clinical, histological, and bacteriological characteristics of all the cases were similar. The lesions were solitary and initially small and single; later, further ulceration occurred near the original site. All were found on the extremities. Each lesion appeared as an inconspicuous, solitary area of slightly inflamed induration in which a small ulceration appeared and then extended indolently. The ulcer was refractile to therapeutic measures which were followed by edema, pyogenic reactions, and often acceleration of the destructive process. Sloughing and denudation of large areas were not accompanied by systemic reaction unless complications occurred. The lesion spread by extension of the marginal induration which subsequently broke down, exposing perpendicular or undermined edges of necrotic tissue. A striking feature was the development from the exposed fascia of a gelatinous mass, "like blubbery granulation tissue." Histological examination of tissue from the ulcer showed necrosis of the ulcer wall, the necrosis being most extensive in fatty tissue in which it extended beneath the dermis. Acid-fast bacilli were found in enormous numbers, in every instance grouped characteristically in sharply defined oval or round masses often as great in diameter as fat cells. Others of the bacilli were in smaller, more scattered groups. No tubercular follicles, giant cells, endothelioid grouping or caseation were seen. Pus from a patient's lesion was treated with sulphuric acid and injected subcutaneously into rats, producing ulceration of the epididymis. Rabbits and mice inoculated intraperitoneally developed similar but less extensive lesions. Acid-fast bacilli were demonstrated in the ulcers of all the animals. Guinea pigs inoculated by either route failed to develop progressive disease. The acid-fast organisms were cultured on such solid media as egg yolk agar, blood agar and the media of Petragnani, Loeffler, and Dorset. The optimum temperature for growth was 30

to 33° C.—*A New Mycobacterial Infection in Man: I. Clinical Aspects, P. MacCallum; II. Experimental Investigations in Laboratory Animals, J. C. Tolhurst & G. Buckle; III. Pathology of the Experimental Lesions in the Rat, H. A. Sissons; IV. Cultivation of the New Mycobacterium, G. Buckle & J. C. Tolhurst, J. Path. & Bact., January, 1948, 60: 93.*—(*H. J. Henderson*)

Spontaneous Pneumothorax.—In 1943 the United States Army had 873 hospital admissions for simple benign spontaneous pneumothorax. It has become apparent in recent years that this type of pneumothorax is relatively common, especially in healthy young adult males. Pleural fluid is slight, fever is uncommon, and uncomplicated re-expansion is the rule. Sixty-three cases are reported in detail. Half of the patients were between 20 and 30 years of age; the ratio of males to females was 5 to 1. In 70 per cent the time required for re-expansion was seven weeks or less but, in any particular patient, it was difficult to predict the time which would be required. In only 3 per cent physical exertion preceded the onset of the pneumothorax. Chest pain occurred in all and subsided in a few days. Dyspnea was present in 83 per cent; 5 patients were slightly cyanotic at the onset. Four patients had no pleural fluid; two had fluid above the diaphragm and in both cases gross blood was aspirated. No patient had pleural adhesions demonstrable on chest X-ray, in sharp contrast to patients with active pulmonary tuberculosis. The sedimentation rate was normal in 73 per cent and slightly elevated in 27 per cent of the cases. Of those who had white blood counts on admission, 70 per cent were normal and the others showed only slight elevation. Most patients were afebrile but two had fever for more than one week. They both had thrombophlebitis. Recurrences occurred in 19 per cent, usually on the same side, but the prognosis was excellent.—*Benign Idiopathic Spontaneous Pneumothorax, A Review of Sixty-three Cases.—B. Hyde & L. Hyde, Am. J. M. Sc., April, 1948, 215: 427.*—(*G. F. Mitchell*)

Spontaneous Mediastinal Emphysema.—A 23 year old man developed pain in the left chest which radiated to the left shoulder and left arm. He became dizzy, nauseated and went into shock. Auscultation revealed a crunching sound over the heart during systole and diastole. The diagnosis of acute myocardial infarction was made. A chest roentgenogram (posteroanterior view) taken a few days later showed no abnormality. A few weeks later the patient developed similar signs and symptoms. A lateral chest roentgenogram revealed an area of increased translucency anterior to the heart. The diagnosis of recurrent spontaneous mediastinal emphysema was made.—*Recurrent Spontaneous Mediastinal Emphysema Simulating Myocardial Infarction, P. C. Pellegrino & E. N. Silber, Am. Heart J., September, 1948, 36: 447.*—(*G. C. Leiner*)

Suppurative Bronchopneumonia. — The authors saw approximately 3,500 cases of pneumonia at a naval hospital during the winter and spring of 1944–1945. Seven cases of bronchopneumonia were characterized by parenchymal suppuration and necrosis with cavity formation and are reported in some detail. Other investigators have reported an equal incidence in the sexes and an occurrence in all age groups, but there appears to be a preponderant frequency in children and young adults. In 4 of the authors' cases, a pure culture of beta hemolytic streptococcus was found; in the other 3 no pathogenic organisms were identified. The clinical symptoms of suppurative bronchopneumonia are fever, cough and expectoration of purulent sputum, with a frequent history of antecedent upper respiratory tract infection. Pleuritic pain is common. There are 4 clinical types of suppurative bronchopneumonia: (*1*) An ordinary bronchopneumonia except for the roentgenographic demonstration of a cavity. Recovery is usually uneventful. (*2*) A more severe, protracted disease which tends to

spread to new bronchopulmonary segments. Some patients recover spontaneously after weeks or months of prolonged relapsing illness. In others, chronic bronchiectasis develops secondary to the pulmonary suppuration and the superimposed atelectasis with its resultant interstitial fibrosis. (*3*) Bronchopneumonia with local surgical complications such as aerobic pulmonary abscess or pleural involvement with empyema or pyopneumothorax. (*4*) Bronchopneumonia in which general or regional spread occurs with cerebral involvement, diffuse septic embolic phenomena, mediastinitis or pericarditis. The cardinal feature of the roentgenographic findings is the presence of one or more areas of cavitation within an area of pneumonic consolidation. The early appearance of a cavity with a sharply defined border and an air-fluid level usually makes differentiation possible. The diagnosis of suppurative bronchopneumonia usually is made without difficulty from the clinical and roentgen findings. However, the more severe forms must be distinguished from other diseases such as pulmonary tuberculosis, putrid lung abscess, bronchogenic carcinoma, actinomycosis and primary atypical pneumonia. Pulmonary abscess incidental to extensive necrosuppurative bronchopneumonia and pulmonary abscess as the predominant feature with a surrounding necrosuppurative pneumonic infiltration require no surgical intervention. The disease usually resolves spontaneously; less frequently it eventuates in bronchiectasis. The pulmonary and pleural complications, however, may require surgical management. The use of penicillin has resulted in a marked reduction in toxicity and may have prevented the occurrence of the more serious complications. — *Suppurative Bronchopneumonia with Cavitation, S. P. Perry & R. Shapiro, Radiology, March, 1948, 50: 351.—(G. F. Mitchell)*

Acute Benign Dry Pleurisy.—An outbreak is described in which 5 nurses and one ward maid at a hospital were affected. All the cases appeared within six days of each other. The affected persons worked in scattered parts of the hospital. The duration of the disease was seven to fourteen days with an average of nine. Chest pain was present in every case and signs of dry pleurisy in 3. Fever ranged up to 103°F and lasted about five days. The elevation in pulse rate was proportional to the fever. In one of the cases there was an area of hyperaesthesia on the chest wall. Roentgenograms were normal. Two cases showed a neutropenia. Sedimentation rates were normal.—*Acute Benign Dry Pleurisy, J. D. Gray & F. S. Carter, Lancet, July 31, 1948, 2: 254.—(A. G. Cohen)*

Calcium Gluconate for Pleuritic Pain.—Clinical observations have indicated that the origin of pleuritic pain is more complex than simple friction between the pleural surfaces. The relief of acute pleural pain by the intravenous injection of calcium gluconate is reported. Ten to 20 ml. of a 10 per cent solution were given in two to four minutes. All but 3 of 30 patients experienced definite relief, the effect being evident in about sixty seconds. Any residual pain was described as a dull aching and unrelated to breathing. Two of the 3 patients obtaining no relief were not benefited by procaine block of the intercostal nerves. Only 4 patients were completely relieved and there was a gradual return of pain in thirty to sixty minutes. Tenderness and hyperasthesia of the chest wall or upper abdominal muscles also disappeared to reappear with the return of pleuritic pain. Ten patients given a second injection were again relieved. The practical value of the treatment lies in its simplicity and its usefulness when examination of the patient is difficult or when he cannot cough to obtain sputum for examination. In 1940 Buchtal reported electromyographic studies of patients with painful muscles and demonstrated that various drugs, including calcium salts, brought about the relaxation of muscle spasm. Other reports emphasize that calcium injection aids in the restoration of normal muscle tone. Several investigators have demonstrated the relief of pain by the local injection of procaine, one injection often

giving permanent relief. Kelly was able to relieve pain in both acute pleuritis and fibromyositis in t' manner. Dybdahl relieved pleuritic pain by spraying ethyl chloride on the skin over the painful area. The authors report success with this method also, the spray being used for twenty to thirty seconds. These results may be explained by the so-called "chain" effect of muscle spasm described by Payr. Pain originating anywhere in the "chain" leads to painful muscle spasm and the pain of spasm induces still more spasm and pain. Thus, if the chain is broken at any point, the spasm is relieved. The relief of painful muscle spasm by the use of erythriodine in anterior poliomyelitis and the relief of painful muscle spasm by curare has been repeatedly demonstrated. Thus, much of the pain of pleuritis may be due to painful spasm of the intercostal muscles which perpetuates itself in a vicious cycle of spasm, pain and more spasm. Relief by any method seems to depend upon interruption of the cycle at some point.—*Pleuritic Pain: Use of Intravenous Calcium Gluconate in Its Relief, I. L. Bennett & W. Lathem, Am. J. M. Sc., April, 1948, 215: 431.*—(*G. F. Mitchell*)

Boeck's Sarcoid.—This report is derived from the study of 7 cases of Boeck's Sarcoid, including one death and autopsy. All the patients were young adults and 4 were Negroes. Five patients had widened hilar shadows on roentgenograms. Tuberculin tests were done on 6 patients and were negative in all. The sedimentation rate was elevated in 5 and remained so for prolonged periods; this test may measure the activity of the disease. In the 2 patients on whom serum protein determinations were carried out, the globulin fraction was above normal. Final diagnosis depends upon histological study of a biopsy specimen, usually an enlarged peripheral lymph node. Several biopsies may be necessary. In one patient, the diagnosis was established by biopsy of a nodule in the biceps muscle. One patient died suddenly at a time when he appeared to be improving and was symptom free. The striking postmortem finding in this man was extensive sarcoid infiltration of the myocardium. He had maintained a pulse rate of 90 to 120 even when afebrile. In retrospect, the authors feel that persistent tachycardia should arouse suspicion of myocardial involvement in Boeck's sarcoid. One other patient with persistent tachycardia manifested electrocardiographic findings indicative of myocardial damage.—*Boeck's Sarcoid: Observations of Seven Patients, One Autopsy, G. S. Bates & J. M. Walsh, Ann. Int. Med., August, 1948, 29: 306.*—(*H. R. Nayer*)

Histoplasmosis and Torulosis of Adrenals.—Tuberculosis has long been recognized as the most frequent infectious cause of adrenal insufficiency though other organisms may produce the same signs and symptoms. Despite their relative infrequency, fungus diseases, especially histoplasmosis and torulosis, should be kept in mind in the differential diagnosis. All the available cases of adrenal involvement by histoplasmosis and torulosis are reviewed. In all, 19 cases of involvement due to Histoplasma capsulatum have been reported. Some symptoms of adrenal insufficiency are reported but for the most part they are masked by complaints referable to other organs. Autopsy showed marked enlargement and parenchymal replacement by yellowish-gray fibrocaseous tissue containing the causative organism. Only 8 cases of adrenal insufficiency due to Torula histolytica have been reported. Two new cases, one of histoplasmosis and one of torulosis are reported by the authors. The symptoms of adrenal insufficiency were recognized in one of the cases prior to death. As in tuberculosis, the ratio of cases of adrenal failure due to histoplasmosis is 2 males to 1 female; 76 per cent of the histoplasmosis cases and only 28 per cent of adrenal torulosis cases showed caseation. The authors suggest that the caseous reaction may be an allergic one.—*Histoplasmosis and Torulosis as Causes of Adrenal Insufficiency, A. J. Rawson, L. H. Collins, & J. L. Grant, Am. J. Med., April, 1948, 215: 363.*—(*G. F. Mitchell*)

Arterio-venous Aneurysm of the Lung.—Two cases of arterio-venous aneurysm of the lung are reported, making a total of 25 cases on record. The outstanding feature is cyanosis. Dyspnea appears later and is progressive. It is probably due to stimulation of the respiratory center by the high carbon dioxide content of the arterial blood and not to cardiac failure. Cerebral anoxemia is responsible for the transient attacks of vertigo, faintness or convulsions which may occur. Pulmonary hemorrhage is frequent; capillary hemangiomata of the skin and mucous membranes are seen often. Clubbing of the fingers is common; hypertrophic osteoarthropathy is rare. There are no abnormal cardiac findings; blood pressure readings are normal. A murmur over the tumor is heard in about half of the cases. Secondary polycythemia and greatly diminished oxygen saturation of the arterial blood is characteristic. An opaque shadow representing the tumor is seen in the lung and may be connected to the hilus by vessels. It may decrease in size with Valsalva's experiment or increase in size when the patient attempts forced inspiration with mouth and nose closed. The lesion is a developmental malformation. The treatment is surgical removal by local excision, pneumonectomy or lobectomy. — *Arterio-venous Aneurysm of the Lung, C. G. Barnes, L. Fatti & D. M. Pryce, Thorax, September, 1948, 3: 148.*—(*A. G. Cohen*)

Lobar Adenocarcinoma.—The autopsy findings in 2 cases with extensive pneumonic consolidations are presented. In a 31 year old woman, diffuse adenocarcinoma of the right lung, with metastases to the left lung, hilar lymph nodes, adrenal gland and kidney was found. In a 73 year old woman the autopsy revealed diffuse adenocarcinoma of the right lung, with metastases to the left lung, hilar lymph nodes, adrenal glands and liver. No distinct point of origin of the tumors was found. The following conclusions are made: "(*1*) The growths are primary in the lung, but metastases from a latent primary glandular focus outside the lung should be carefully excluded. (*2*) They arise from the mucosa of the bronchial tree beyond the larger bronchi, the point of origin being obscured by the extensive growth involvement. (*3*) A source of origin from pre-existing epithelized alveoli cannot be proved. (*4*) A multicentric origin cannot be established. (*5*) To date there is no proved relationship between diffuse adenocarcinoma of the lung and pulmonary adenomatosis."—*Lobar Adenocarcinoma of the Lung Simulating Pneumonia. Report of Two Cases, G. Silverman & A. Angrist, Arch. Int. Med., March, 1948, 81: 369.*—(*G. C. Leiner*)

Horner's Syndrome from Osteochondroma.—Horner's Syndrome may be produced by any type of apical lung tumor but is most commonly associated with malignant neoplasms. The author reports the case history of a 34 year old woman in whom the syndrome had been present for twenty years. Intermittent gnawing pain in the left arm had been present since the age of seven. Chest X-ray revealed a left apical mass with irregular calcification and a clearly demarcated outer margin. A hard bony mass was palpable in the left supraclavicular fossa. At operation the tumor mass was found to arise from the first rib and was completely removed. The pathological diagnosis was osteochondroma. Eight months after removal, there was evidence of some regeneration of the sympathetic fibers. Horner's Syndrome produced by osteochondroma of left first rib is an extremely rare finding.—*Horner's Syndrome Due to An Osteochondroma of the First Rib, J. F. Simpson, Canad. M. A. J., August, 1948, 59: 152.*—(*H. R. Nayer*)

Roentgenography of the Diaphragm.—The diaphragm, both anatomically and physiologically, is a vulnerable structure, being readily involved by pathological changes arising from above and below or from inherent weaknesses of the structure itself. Roentgenographic studies have paid the greatest attention to the anteroposterior projection, although the surface of the diaphragm is not horizontal throughout. Each leaf has the

shape of a dome, the highest point being medial and anterior with a downward slope in the lateral and backward extensions, so that only the surface of the highest level can be seen in an anteroposterior view. One-third to one-half of the diaphragm lies behind the heart and is not seen at all. Thus, for a satisfactory roentgenographic examination of the entire diaphragm, a lateral as well as a frontal view is essential. This technique has been used successfully for many years and the authors have demonstrated many abnormal conditions which were hardly suspected in the customary frontal projections. The diaphragm, being in intimate contact with the underlying structures, cannot be seen by itself, but the presence of free air within the abdomen enables one to see it elevated, giving a more accurate picture of its position, contour, and thickness. A study of 8 cases showed that the fundamental roentgenographic technique of making two projections at right angles to one another should be applied to the diaphragm to demonstrate satisfactorily its complete topography. It has made possible the recognition and localization (with or without the aid of barium suspension) of herniation through any part of the diaphragm; the differentiation of lesions not seen in the anterior projection; demonstration of elevation of the diaphragm, in whole or in part, often suggestive of intra-abdominal tumors; and finally, the most practical application of all, the diagnosis of subphrenic abscess. This is indicated by elevation of the diaphragm and obliteration of the posterior costophrenic angle producing the "plateau sign of subphrenic abscess."—*The Diaphragm, S. Brown & A. Fine, Radiology, February, 1948, 50: 157.*—*(G. F. Mitchell)*

Pleural Fluid Simulating Elevated Diaphragm.—The author presents 5 cases in which pleural fluid at the lung base closely simulated elevation of the diaphragm, in 2 instances on the right and in 3 on the left. The roentgenographic appearance of the fluid must be distinguished from subphrenic disease (inflammatory or neoplastic), paralysis of the diaphragm, atelectasis, eventration of the diaphragm, and intrapleural or intrapulmonary neoplastic disease. It is most difficult to differentiate between the collection of fluid and a subphrenic disease producing a progressive elevation of the diaphragm. The patients often have fever and vague symptoms which are of little help in localizing the process. The signs on physical examination may be identical in the two conditions. Fluoroscopy, lateral decubitus roentgenograms, pleural tap, demonstration of the stomach bubble, which may be accentuated by giving the patient a carbonated drink prior to examination, and pneumoperitoneum are suggested as useful procedures in differential diagnosis. Among the factors leading to the production of basal fluid accumulations, fibrinoplastic adherence of visceral and parietal layers of the pleura is believed to be of major importance.—*Basal Pleural Fluid Accumulations Resembling Elevated Diaphragms, D. B. Jones, Radiology, February, 1948, 50: 227.*—*(G. F. Mitchell)*

Pleural Fluid Simulating Elevated Diaphragm.—The authors present a typical example of an infrapulmonary effusion masquerading as an elevated diaphragm. A 27 year old white female with bilateral pulmonary tuberculosis complained of pain in the right lower portion of the chest and became slightly febrile. Fluoroscopy revealed an elevated, arched right diaphragmatic leaf which moved over only one interspace. The costophrenic angle was clear and no free fluid was detected. Roentgenograms confirmed these findings. The lower half of the right side of the chest was dull to percussion, with decreased or absent breath sounds. Diagnostic pneumoperitoneum was initiated and demonstrated an infrapulmonary effusion. An anteroposterior roentgenogram of the chest in the right decubitus position revealed a well defined fluid level in the costal gutter, some of the fluid remaining in the infrapulmonary space at the end of five minutes. Diagnostic thoracentesis revealed a clear amber fluid which contained no acid-fast bacilli.—*Infrapulmo-*

nary Effusion Masquerading as an Elevated Diaphragm, J. T. Taguchi & S. Dressler, Radiology, February, 1948, 50: 223.—(G. F. Mitchell)

Diagnosis of Retrocardiac Shadows.—The configuration of the cardiac shadow observed on a routine roentgenogram of the chest was given adequate emphasis and the findings were correlated with electrocardiograms by Master; the variations in density within the triangular shadow have received little consideration unless there was a fluid level or calcification. Systematic analysis of the triangular shadow will frequently disclose considerable variations in density, many of which present characteristic features of diagnostic importance, leading to other diagnostic procedures or aiding in the detection of differential diagnosis and of asymptomatic retrocardiac lesions. The space-occupying lesions located in the upper half of the mediastinum produce pressure signs relatively early and are frequently suspected by the clinician. In the retrocardiac region, where the space is wide, the most obscured thoracic lesions occur and these may reach considerable size before they lead to clinical signs or symptoms. By early detection and proper evaluation of the abnormal retrocardiac shadows, the radiologist may establish the diagnosis before clinical signs and symptoms become apparent. Certain diseases of the stomach, esophagus, aorta, heart, lungs, and vertebral columns cast characteristic retrocardiac shadows which may not project beyond the cardiac outline, but which can be recognized as variations in density within the cardiac shadow. Multiple convex lines within the cardiac shadow indicate the presence of the stomach in the retrocardiac region. A simple double contrast method for the study of the cardiac-esophageal junction and the relationship of the lower third of the esophagus to the stomach is presented.—*Differential Diagnosis of Retrocardiac Shadows, S. S. Nemec, Radiology, February, 1948, 50: 174.—(G. F. Mitchell)*

Visible Bronchial Tree.—The visibility of the air-filled bronchi within parenchymatous consolidations of the lung is explained on theoretical grounds and illustrated by the use of a model made of a box containing two rows of drinking straws; one row, empty, *i.e.*, air filled, and the other filled with paraffin. A roentgenogram of the box showed the paraffin-filled straws as white bands; the empty straws are invisible except for the faint shadows cast by their walls. In a roentgenogram of the box filled with water, the paraffin-filled straws were not detectible; the air-containing straws appeared as dark bands. The "visible bronchial tree" is a helpful sign in the recognition of parenchymatous lesions of the lung, especially of pneumonic consolidation, including tuberculous pneumonia. Infarcts and tumors may also show this sign if the bronchi are not blocked or filled by blood or secretion. In atelectasis due to compression or obstruction, the approximation of the visible bronchi may reveal the atelectatic nature of the process. The "visible bronchial tree" is also helpful in differentiating basal pneumonic consolidations from pleural effusion or thickened pleura. Only the presence of the visible bronchial tree is of diagnostic value; it may be absent in pneumonic consolidation. Failure to demonstrate the bronchi may be due to filling with secretion, edema, or blood, or may be the result of technical errors, such as over or under exposure. The sign is particularly helpful in recognizing faint congestion and faint shadows in pulmonary consolidations. This sign has been found most valuable in pediatric roentgenology.—*The Visible Bronchial Tree, F. G. Fleischner, Radiology, February, 1948, 50: 184.—(G. F. Mitchell)*

Streptomycin-requiring *Mycobacterium Ranae*.—Approximately 25 billion organisms of a streptomycin-resistant strain of *M. ranae* were plated on a deficient medium containing streptomycin. A variant was found which requires streptomycin since neither the parent strain nor the variant grew on the deficient medium alone. If such a variant

can also develop from pathogenic tubercle bacilli, its significance in the chemotherapy of tuberculosis is evident.—*A Variant of Mycobacterium Ranae Requiring Streptomycin for Growth, D. Yegian & V. Budd, J. Bact., April, 1948, 55: 459.*—(*F. G. Petrik*)

Effect of Fluoride on Mycobacteria.—Recently Davis and Dubos have shown that fluoride, in concentrations that do not affect the growth of *M. tuberculosis* H37RV, inhibits the action of lipase on "Tween 80." The present study deals with the effects of the fluoride ion on the metabolism of certain mycobacteria. Most of the experiments were done with a rapidly growing BCG strain of *M. tuberculosis* (ATC 8240). Similar effects were, however, obtained with *M. tuberculosis* (ATC 607) and the strain H37RV. The results showed that the oxygen uptake of washed suspensions of the BCG strain is greatly increased by sodium fluoride and that the amount of increase depends on the relative concentrations of fluoride and bacteria as well as upon the hydrogen ion concentration. The effect is greatest at pH 6.0, intermediate at pH 6.7, and least at pH 7.8.—*The Effect of Sodium Fluoride on the Metabolism of Certain Mycobacteria, R. J. Fitzgerald & F. Bernheim, J. Bact., May, 1948, 55: 677.*—(*F. G. Petrik.*)

Penicillin and Growth of Mycobacterium.—The effect of penicillin on the growth of *M. tuberculosis* was studied using four strains from active human cases in addition to standard laboratory strains of human, bovine and avian type. Crystalline penicillin G sodium (Merck) was used in a culture medium prepared according to the formula of Dubos and Davis. Human, bovine and avian types of *M. tuberculosis* were inhibited by concentrations of penicillin varying from 1 to more than 200 units per ml. depending on the size of the inoculum. Among the human strains, no marked difference in sensitivity was observed between a standard laboratory strain (H37RV) and strains recently isolated. The strains of bovine and avian type were more sensitive to penicillin than human ones.—*The Effect of Penicillin on the Growth of Mycobacterium Tuberculosis in Dubos Medium. M. Solotorovsky, E. J. Bugie & B. M. Frost, J. Bact., April, 1948, 55: 555.*—(*F. G. Petrik.*)

Desensitization and Tuberculin Cytotoxicity.—Tuberculin (OT) caused specific suppression of the initial migration of leucocytes from splenic explants of tuberculous guinea pigs. This suppression was markedly reduced by specific desensitization. This finding indicates that the cytotoxic effect of tuberculin on tissue explants of tuberculin-sensitive animals is the result of the interaction of a sessile antibody with specific antigen.—*Tuberculin Reaction. II. Cytotoxicity of Tuberculin for Splenic Explants of Desensitized Tuberculous Guinea Pigs, W. F. Kirchheimer & R. S. Weiser, Proc. Soc. Exper. Biol. & Med., June, 1948, 68: 407.*—(*F. B. Seibert*)

Synthetic Phthioic Acid.—Certain synthetic fatty acid produced necrosis, abscess formation and foam cell nodules in the omentum, lymph glands and spleen when injected into the peritoneal cavity of the guinea pig. Naturally occurring phthioic acid produced the same reaction.—*The Pathogenic Effect of Phthioic Acid and its Synthetic Analogues, J. Unger, C. E. Coulthard & L. Dickinson, Brit. J. Exper. Path., August, 1948, 29: 322.*—(*H. J. Henderson*)

Enzyme Inhibition by Streptomycin.—Benzoic acid is oxidized by an adaptive enzyme in certain *Mycobacteria*. Streptomycin inhibits this oxidation probably by inhibition of the formation of this enzyme. *Mycobacterium lacticola*, which oxidizes p-hydroxybenzoic as well as benzoic acid itself, was shown to have its ability to oxidize p-hydroxybenzoic acid less inhibited by streptomycin, if it had previously been grown in a medium containing 60 mg. per cent of p-hydroxybenzoate. Growth in benzoic acid increases to a small extent the amount of adaptive enzyme for p-hydroxybenzoic acid and growth in this latter acid has

a somewhat greater effect on the amount of adaptive enzyme for benzoic acid. It is clear that the two acids are oxidized by separate enzymes. Experiments were made with *Mycobacterium tuberculosis* BCG to determine the amount of benzoic acid required by the cell suspension to produce a measurable amount of adaptive enzyme and the time of exposure necessary for the effect to occur. Maximum inhibition by streptomycin occurs if it is added to the bacilli ninety minutes before the benzoate. The authors, however, have not been able so far to demonstrate adaptive enzyme formation in virulent *Mycobacteria* which are sensitive to streptomycin.—*The Inhibition by Streptomycin of Adaptive Enzyme Formation in Mycobacteria, R. J. Fitzergerald, F. Bernheim, & D. B. Fitzgerald, J. Biol. Chem., August, 1948, 175: 195.*—(*F. B. Seibert*)

Chemical Determination of Streptomycin.—A fluorometric method, based on the formation of a fluorescent hydrazone, for the determination of streptomycin in urine and tissue was described. The lower limit of sensitivity was 2 γ per ml. of urine and of tissue. Data on the analytical recoveries of streptomycin added to urine and to lung, liver, brain, heart, and spleen are presented. The utility of the method for the determination of streptomycin in urine and tissues following parenteral administration has been demonstrated.—*A Chemical Determination of Streptomycin in Body Tissues and Urine. V. C. Jelinek & E. Boxer, J. Biol. Chem., August, 1948, 175: 367.*—(*F. B. Seibert*)

Effect of Streptomycin and PAS on Tubercle Bacilli.—The growth of tubercle bacilli (H37RV) on Dubos medium is inhibited by 0.74 γ per cc. of streptomycin or by 1.2 γ of para-aminosalicylic acid (PAS). A moderately inhibiting concentration of either streptomycin or of PAS when combined with a completely noninhibiting concentration of the other drug produces a marked enhancement of inhibition of the growth *in vitro* of H37RV. *In vitro* growth of a resistant strain of human tubercle bacilli (H37RVNR1) is inhibited by 1.2 γ per cc. of PAS, and this inhibition is not enhanced by the addition of streptomycin.—*In vitro Effect of Streptomycin and Para-Aminosalicylic Acid (PAS) on the Growth of Tubercle Bacilli, K. Vennesland, R. H. Ebert & R. G. Bloch, Proc. Soc. Exper. Biol. & Med., June, 1948, 68: 250.*—(*F. B. Seibert*)

Streptomycin for Bone Tuberculosis.—Sixteen patients with tuberculosis of the bones and joints have been treated with streptomycin. Nineteen joints were involved. Sinuses were present in 4 patients. The period of observation following discontinuation of streptomycin therapy varied from one to eighteen months. In addition to streptomycin therapy, other forms of treatment were carried out whenever indicated. Response to streptomycin was favorable in 9 patients and fair in one patient. Four patients showed no benefit while treatment was too recent to permit valid conclusions in 2 patients. The daily administration of 1 Gm. of streptomycin for ninety days is considered a satisfactory course of treatment.—*Streptomycin in Tuberculosis of Bone and Joint, W. H. Bickel, H. H. Young, K. H. Pfuetze & T. Norley, J.A.M.A., June 19, 1948, 137: 682.*—(*H. Abeles*)

Streptomycin for Pulmonary Tuberculosis.—The authors outline some tentative clinical interpretations with regard to the use of streptomycin in pulmonary tuberculosis. Conclusions are based on their own experience and on direct knowledge of the work of others. In acute febrile tuberculosis, symptomatic response is often striking and may occur within three to four days, much before any changes in the specific lesions can be noted. Local symptoms, such as the pain of tuberculous laryngitis, cough or urinary symptoms may subside rapidly. Acute tuberculous lesions in the lung and larynx may show accelerated resolution under the influence of the antibiotic which suppresses bacterial growth before caseous necrosis has set in. Although complete clearing roentgenographically may occur, the likeli-

hood of persistent minute caseous foci must be assumed. Resolution of acute pulmonary lesions may proceed for several months after completion of a course of streptomycin. The presence of caseation limits, to a large extent, the response to streptomycin. In extensive caseous lesions, there may be early symptomatic response but little objective evidence of resolution and early relapse is common. The frequent finding of a caseous cerebral focus in tuberculous meningitis probably explains the high incidence of relapse and the fatality rate (approximately 80 per cent) after initial improvement. Definitive arrest of the tuberculosis still depends primarily on the slow healing and fibrosis of caseous disease. In spite of immediate favorable effects, streptomycin has, therefore, not shortened the time required for ultimate healing. Streptomycin may aid in restoring a favorable balance but the natural resistance of the patient remains of great importance. The greatest benefit from the drug may be obtained when it is employed in association with rigid rest. The partial improvement obtained with streptomycin may render surgical measures possible in previously hopeless cases. Drug-resistant bacilli appear within four weeks and are found in 70 per cent or more of patients within three to four months. Resistance appears to be more directly related to the duration of treatment than to the daily dosage. The authors' experience indicates that treatment for a period of six weeks with doses of 1 to 2 Gm. daily may be as effective as longer periods. Under the six week regimen, drug-resistance appeared in 25 to 30 per cent of the patients; the drug is, therefore, effective in the majority of these patients if further treatment is needed. In 12 of 18 patients, the authors observed complete loss of labyrinthine function when a dosage of 2 Gm. a day for six weeks was employed. Administration of 1 Gm. a day for six weeks did not destroy vestibular function although there was occasional partial impairment. In cases of generalized hematogenous tuberculosis and tuberculous meningitis, where the fatality rate is very high, treatment should be carried out for ninety days in daily doses of 40 mg. per kg. of body weight, and the disadvantages of drug toxicity and bacterial resistance should be ignored. In meningitis, 50 mg. of the drug should be given intrathecally at twenty-four to seventy-two hour intervals during the ninety days. The value of concomitant administration of the sulfones and para-aminosalicylic acid requires further evaluation. In every patient in whom the use of streptomycin is contemplated, careful consideration should be given to possibility of more critical future episodes. In milder cases it may be wise to administer the drug only for short periods or to withhold it entirely for the time when it may be needed most urgently.—*Streptomycin in the Treatment of Tuberculosis, J. B. Amberson & W. H. Stearns, Ann. Int. Med., August, 1948, 29: 221.*—(*H. R. Nayer*)

Superinfections during Antibiotic Therapy.—Two patients with pneumococcic pneumonia were given penicillin therapy during the course of which new infections due to gram-negative bacilli appeared. Both patients responded to streptomycin therapy. The mechanism by which the new infection occurs is not clear but it may be due to a disturbance in the degree of bacterial antagonism which is normally present. The importance of frequent bacteriologic examinations before and during treatment with an antibiotic is stressed. It is not advisable to start treatment with a combination of penicillin and streptomycin.—*Occurrence of Superinfections during Antibiotic Therapy, E. Appelbaum & W. A. Leff, J. A. M. A., September 11, 1948, 138: 119.*—(*H. Abeles*)

Streptomycin in Pregnancy.—Two patients, both in the second trimester of pregnancy, were treated with streptomycin. One patient had tuberculosis of the urinary tract and the other had far advanced pulmonary tuberculosis. Both patients gave birth to normal infants without neural defects. The placenta was normal in both cases.—*Streptomycin Therapy, Effects on Fetus, E. H. Watson &*

R. M. Stow, J. A. M. A., August 28, 1948, 37: 1599.—(H. Abeles)

Chemotherapy for Pulmonary Infections.—The number of postoperative pulmonary infections following major abdominal and thoracic procedures was greatly reduced by inhalation of relatively small doses of micronized penicillin or streptomycin mixtures during the operative and postoperative period. —*Prevention of Postoperative Pulmonary Infections, Inhalation of Micropowdered Penicillin and Streptomycin, G. V. Taplin, S. H. Cohen & E. B. Mahoney, J. A. M. A., September 4, 1948, 138: 4.—(H. Abeles)*

Sulphetrone for Tuberculosis.—Sulphetrone was administered to patients with pulmonary tuberculosis considered unsuitable for other forms of active therapy. The dose was 3 Gm. daily, given in tablets of 0.5 Gm. every four hours for about a week. Thereafter, the daily dose was gradually increased to 5 to 8 Gm. daily. Fluids were limited to 1,500 cc. daily and alkali was given with each dose. The patients were continued on the drug indefinitely. No beneficial effect was noted in cases of tuberculous meningitis, miliary disease or bronchopneumonia. Only one patient with very far advanced disease was benefited. Patients with somewhat less advanced disease often showed considerable improvement. The most frequent toxic effect was the appearance of anemia. Other side effects were headache, nausea, vomiting and rashes.—*Chemotherapy of Pulmonary Tuberculosis with Sulphetrone, T. Anderson & S. J. Strachan, Lancet, July 24, 1948, 2: 135.—(A. G. Cohen)*

Sulphetrone for Tuberculosis.—A total of 44 cases of tuberculosis, of which 42 were pulmonary, were treated with sulphetrone. There was improvement in 22, no change in 5, progression in 6 and death in 11 cases. The improvement was considerable in 9, moderate in 7 and slight in 6. It was not dramatic in any case.—*Chemotherapy of Tuberculosis with Sulphetrone, M. G. Clay & A. C. Clay, Lancet, July 31, 1948, 2: 180.—(A. G. Cohen)*

Sulphetrone for Tuberculosis.—Seventy cases of pulmonary tuberculosis were treated with sulphetrone. Prior to treatment, ferrous sulphate and brewer's yeast were administered for two weeks. The patients were kept in bed. The objective was attainment of a blood level of from 7.5 to 10 mg. per cent. A level greater than 12.5 mg. per cent was dangerous. Because early doses are not well tolerated, these were small and were increased gradually. The drug was given intramuscularly in miliary tuberculosis and tuberculous meningitis. The patients were watched for the appearance of anemia. Minor toxic symptoms were headache, nausea, mental depression and cyanosis. Danger signals were continuous headache, nausea, vomiting, vertigo and mental confusion. Treatment lasted from a few days to eighteen months. There were no beneficial effects in miliary tuberculosis or tuberculous meningitis. Improvement was seen in 12 of 17 cases of acute fibrocaseous tuberculosis and in 13 of 22 chronic cases. Each of 4 cases of primary pulmonary tuberculosis and 6 of 8 cases of strictly exudative disease were improved. In the chronic hematogenous type all 4 cases were improved, as were 3 of 4 cases of productive tuberculosis. In every case, the trend in exudative cases was halted and reversed.—*Treatment of Tuberculosis with Sulphetrone, D. G. Madigan, Lancet, July 31, 1948, 2: 174. —(A. G. Cohen)*

Experimental Chemotherapy in Mice.—A review of the literature on the use of the mouse in the study of experimental tuberculosis convinced the authors that mouse tuberculosis has not been sufficiently delineated for practical purposes. When appropriate allowances are made for several variables, however, a common pattern begins to emerge. It was concluded that: (*1*) the white mouse is more resistant to tuberculous infection than most mammalian species; (*2*) it can be easily and regularly infected with the mammalian and avian varieties of *M. tuberculosis* by a variety of routes; (*3*) the lesions produced are quite diversified and are not histologically

identical with those described for other species; and (4) the particular histoarchitecture observed depends upon the variety, virulence and dose of infecting organism, the route of inoculation, and the time of observation. It is apparent that the histopathologic picture produced by a given set of the foregoing variables must be standardized before its alteration by any therapeutic agent can be evaluated.—*The Use of Mice in Experimental Chemotherapy of Tuberculosis: I. Rationale and Review of the Literature. G. W. Raleigh & G. P. Youmans, J. Infect. Dis., May–June, 1948, 82: 197.*—(*F. G. Petrik*)

Experimental Tuberculosis in Mice.—The evolution of mouse tuberculosis under standardized experimental conditions is described. The clinical and histopathologic pattern is defined and it is felt that potential therapeutic agents can be recognized by the alterations they induce in this pattern. *The Use of Mice in Experimental Chemotherapy of Tuberculosis: II. Pathology and Pathogenesis. G. W. Raleigh & G. P. Youmans, J. Infect. Dis., May–June, 1948, 82: 205.*—(*F. G. Petrik*)

Experimental Chemotherapy in Mice.—Twenty potential chemotherapeutic agents were administered to tuberculous mice. Under aseptic precautions 0.1 mg. of virulent human type tubercle bacilli was injected intravenously into mice of the Strong A strain weighing between 20 and 25 Gm. The compounds were administered to the mice by admixture with the diet, except streptomycin which was given subcutaneously. The compounds tested were selected either on the basis of *in vitro* bacteriostatic tests or on the basis of known chemotherapeutic action. Administration of each drug was begun two to three days before the animals were infected with tubercle bacilli and was continued with all compounds, except streptomycin, for twenty-eight days. Streptomycin treatment was started on the day of infection and extended over 35 days. Treated mice were compared in every respect with homologous control animals infected at the same time. Of the 20 compounds tested only streptomycin and para-aminosalicylic acid were found to be appreciably effective. It is felt that survival time, weight change and the histopathologic picture constitute a triad of useful measures in the assay of any chemotherapeutic agent and that of these three determinations the latter is most important.—*The Use of Mice in Experimental Chemotherapy of Tuberculosis: III. The Histopathologic Assay of Chemotherapeutic Action, G. P. Youmans & G. W. Raleigh, J. Infect. Dis., May–June, 1948, 82: 221.*—(*F. G. Petrik*)

Aerosol Antibiotic Administration.—The efficacy of nebulization therapy depends on the local effect of the antibiotic in the bronchial tree and is not dependent on the absorbtion of the antibiotic by the blood. Penicillin "aerosol" therapy is indicated for infections of the tracheobronchial tree caused by bacteria which are sensitive to penicillin; streptomycin "aerosol" is indicated for those infections caused by streptomycin-sensitive organisms. Penicillin and streptomycin "aerosols" have proved to be of greatest value in the eradication of purulent exudates complicating bronchiectasis. The method has been of particular value in the preoperative preparation of patients for lobectomy. "Aerosols" of penicillin or streptomycin are sometimes helpful in the treatment of nontuberculous lung abscess. Their value is limited by the difficulty in getting the drug into the diseased portion of the lung. Nebulization therapy may be helpful in treating patients with asthma, emphysema, and chronic bronchitis only if these conditions are associated with infections of the bronchial tree caused by bacteria sensitive to the antibiotic used. "Aerosols" are of no value in treatment of respiratory infections caused by viruses.—*Administration of Antibiotic Preparations by the Aerosol Method: A Critical Evaluation, A. M. Olsen, Medical Clinics of North America, July, 1948, 32: 1077.*—(*L. Hyde*)

Postural Changes in Vital Capacity.—The vital capacities were determined in 9 adult

male subjects in the standing and supine positions. Cuffs placed at the bases of the arms and legs were inflated to diastolic pressure, above systolic pressure, or left uninflated. If the cuffs were inflated to a level above the systolic blood pressure with the subject standing, the reflux of venous blood from the trunk and head did not lower vital capacity when he reclined. There was no difference between the vital capacity of a subject standing with the cuffs inflated above the systolic pressure and the vital capacity of the same subject standing with noninflated cuffs.—*Postural Changes in Vital Capacity with Differential Cuff Pressures at the Bases of the Extremities, G. S. Campbell & R. B. Harvey, Am. J. Physiol., March 1, 1948, 152: 671.*—(*G. C. Leiner*)

Residual Air.—The residual lung volume was determined in 6 trained subjects with the "nitrogen dilution method" in which the nitrogen in the residual air is diluted by rebreathing a known volume of oxygen, and by two new methods. (*1*) On the "helium substitution method" the residual air of the lungs is replaced by a known helium-oxygen mixture. The helium is then washed out of the lungs by inhalation of air or oxygen and its volume measured. (*2*) In the "volume expansion method" measurements are made of the increase in gas volume which results from the expansion of the residual air when the ambient pressure is rapidly reduced from 4 to one atmospheres. The mean residual air in the 6 subjects as determined by the nitrogen dilution method was 1,491 cc., by the helium substitution method 1,427 cc., by the volume expansion method 1,429 cc.—*Residual Lung Volume Determinations by the Methods of Helium Substitution and Volume Expansion, T. L. Willmon & A. R. Behnke, Am. J. Physiol., April 1, 1948, 153: 138.*—(*G. C. Leiner*)

Intra-alveolar Pressure.—The roentgenographic appearance of the lungs is dependent to a great extent upon the degree of filling of the pulmonary vessels. With an increase in filling, the lung pattern becomes more prominent; with a decrease, it becomes less prominent. The intra-alveolar pressure, by influencing the filling of the vessels, affects the appearance of the lungs. Variations in the intra-alveolar pressure also produce an effect upon the circulation and, in consequence, upon the heart. During routine roentgenography of the lung, there may be marked variations in the intra-alveolar pressure. Laurell has shown that roentgenograms are comparable only when the same intra-alveolar pressure is present each time the lung is examined. The author used a manometer attached to a mouthpiece to measure intra-alveolar pressure and made roentgenograms at different pressures. The volume of the heart increases one-third when the alveolar pressure is low and decreases one-third when it is high. In normal persons a positive pressure of 40 cm. of water is needed to compress visibly the central branches of the pulmonary artery and this pressure corresponds to the intravascular pressure in the pulmonary artery. Thus a rough estimate of the pressure in the pulmonary arteries can be obtained by determining the intra-alveolar pressure at which the arteries in the hilum are reduced in size. Though this may be a rough method of determining the pulmonary arterial pressure, it is of practical importance for the determination of the degree and the prognosis of mitral valvular disease and may also be of value in the diagnosis of other diseases causing increased blood pressure in the pulmonary artery. A high intra-alveolar pressure, compressing the central branches of the pulmonary artery, aids in demonstrating the hilar lymph nodes on the chest roentgenogram. In a study of primary tuberculosis, hilar node enlargement was demonstrable in 62 per cent of the cases. In a later series of cases studied with both normal and high intra-alveolar pressures, an enlargement of the hilar nodes was found in 97 per cent of the cases. In pulmonary stasis the widened vascular shadows and the opacities caused by pulmonary edema decrease considerably with high intra-alveolar pressure; in some cases the appearance of

stasis may be entirely obliterated while in others it becomes less pronounced. In cases of acute bronchopneumonia the diffuse, opaque network of the parenchyma appears thinner and the opacity is less pronounced but more sharply defined in films made at high pressure. Altering the intra-alveolar pressure causes little or no change in the roentgenographic appearance of acute lobar pneumonia, acute and chronic atelectasis, chronic pneumonia and in most cases of tuberculosis. Cases illustrative of the various types of pulmonary disease discussed are presented.—*The Importance of Intra-alveolar Pressure in the Diagnosis of Pulmonary Diseases, N. Westermark, Radiology, May, 1948, 50: 610.*—(*G. F. Mitchell*)

Pulmonary Edema.—The intracranial pressure was increased in dogs up to over 300 mm. of mercury. This did not cause pulmonary edema. However, a condition resembling pulmonary edema may be produced in such experiments due to the aspiration of saliva.—*An Attempt to Produce Pulmonary Edema by Increased Intracranial Pressure, A. Surtshin, L. N. Katz & S. Rodbard, Am. J. Physiol., March 1, 1948, 152: 589.*—(*G. C. Leiner*)

Pulmonary Arterial Blood Pressure.—In anesthetized cats, measurements of the pressure in the pulmonary artery were made by means of a cannula inserted into the pulmonary artery. In some instances there were indications of a nervous influence on the pulmonary arterial pressure. Inhalation of carbon dioxide produced increase in the pressure; oxygen want had a similar but stronger effect. Oxygen inhalation produced a drop of the pressure. Increase of inspiratory or expiratory resistance increased the pulmonary arterial pressure. The blood flow through any part of the lungs depends on its ventilation, the flow shifting from badly ventilated parts of the lungs to parts which are well ventilated.—*Regulation of Pulmonary Arterial Blood Pressure, G. Liljestrand, Arch. Int. Med., February, 1948, 81: 162.*—(*G. C. Leiner*)

Pulmonary Vascular Diseases.—The causes of peripheral vascular disease of the lung may be grouped as follows: (*1*) intrinsic disease of the vessel wall or obstruction of the lumen; (*2*) changes in vessels produced by adjacent disease of the pulmonary parenchyma; and (*3*) toxic and hypersensitivity states resulting in increased permeability of vessel walls. Arteriosclerosis, arteriolosclerosis and pulmonary hypertension cause changes in the pulmonary vessels. Obliterative vascular disease regularly accompanies advanced pulmonary emphysema. Obstruction of the vascular lumen may be due to a great variety of conditions: foreign material, septic, organic, or inorganic fragments circulating in the systemic blood vessels, neoplasms, blood dyscrasia, and parasitic infestations. Vascular changes are produced by the adjacent disease in acute pneumonia, in chronic inflammatory conditions and neoplasms, in tuberculosis and in silicosis. Some pathologic lesions are associated with a great variety of conditions: poisoning with sulfonamide compounds, serum sickness, eczema, lupus erythemathosus, acute rheumatic fever, and periarteritis nodosa. If sensitization becomes profound, organic destruction of the vessel wall occurs with necrosis. The effects of exogenous and endogenus toxins on the walls of small vessels are identical with the manifestations of hypersensitivity. Vascular permeability may be altered in long standing protein deficiency, in beri-beri, and in a peculiar iron deficiency described by Waldenstrom.—*Peripheral Vascular Disease in the Lung, Roentgenologic Manifestations, R. P. Barden & D. A. Cooper, J. A. M. A., June 12, 1948, 137: 584.*—(*H. Abeles*)

Laryngeal Swab in Pulmonary Tuberculosis.—In 201 patients with radiological evidence of tuberculosis but with no sputum or with no demonstrable tubercle bacilli in the sputum, cultures were made of gastric contents and laryngeal swabs. Gastric lavage was slightly superior for obtaining cultures of tubercle bacilli from inpatients; there was no difference in the results of the 2 methods for

outpatients. Laryngeal swabs are preferred by patients and are less laborious for physicians, nurses and laboratory technicians.—*Laryngeal Swab in Early and Convalescent Cases of Pulmonary Tuberculosis, G. B. Forbes, B. J. D. Smith, J. V. Hurford & V. H. Springett, Lancet, July 24, 1948, 2: 141.*—(*A. G. Cohen*)

Tuberculin Testing.—Tuberculin testing will be very important in the proposed BCG inoculation programs, since it will be necessary to determine which persons are to be vaccinated and to follow those who have been vaccinated. The only immediate and tangible evidence of any change in the immune mechanism is the reversal of the tuberculin reaction from negative to positive. There is a tendency for the cutaneous sensitivity to tuberculin to disappear in cases of healed tuberculosis. The frequency of this reversal is definitely related to the degree of sensitivity exhibited by the patient on the original test. Of 2,490 persons with positive tuberculin tests who were followed for five to fifteen years, 11 per cent lost their tuberculin sensitivity. This occurred much more frequently in persons whose sensitivity was low initially, and most often in children; a similar reversal was observed rarely in adults. Clinical evidence has been accumulated to show that a tuberculous patient who has overcome his infection may completely lose his cutaneous sensitivity but retain his acquired resistance to the disease. Immunity against tuberculosis in such a patient is different from the immunity of a person who has never been infected and who reacts negatively to intradermal tuberculin. Animal experiments support this thesis. Statistical conclusions drawn from tuberculin surveys made twenty or thirty years ago are no longer valid. New country-wide surveys of varied adult groups are indicated. The tuberculin skin test is becoming an important aid in general diagnosis especially when one deals with puzzling diseases of the thorax.—*Changing Concepts in Tuberculin Testing, G. G. Stilwell, Medical Clinics of North America, July, 1948, 32: 1095.*—(*B. Hyde*)

Tuberculosis in Students.—Since 1929 the University of Minnesota Students' Health Service has tested all medical students with tuberculin and made chest roentgenograms of all reactors. In 1936 over 65 per cent of the nonreactors on entrance became reactors while in school. Following the introduction of a control program, this percentage fell to 3.2 per cent in 1947. There was no significant difference in the development of the chronic reinfection type of tuberculosis among those entering as reactors and those who became reactors while in school.—*Prevention of Tuberculosis Among Students of Medicine, H. S. Diehl, R. E. Boynton, S. Geist-Black & J. A. Myers, J.A.M.A., September 4, 1948, 138: 8.*—(*H. Abeles*)

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"In all cases where P.A.S. has been tried the picture has followed the same pattern—loss of toxicity, control of pyrexia and cough, increased appetite, and gain in weight. Some of the patients are now fit for surgical treatment. The remainder, unsuitable for surgery, will soon present the problem of what is to be done with them. Will they get along as inactive open cases, or will further courses of P.A.S. be needed to ensure a reasonable span of life? I feel that in earlier cases, with less gross destruction of the lung, P.A.S. may well afford a complete cure. It also seems that the daily dose must be greatly increased—to not less than 20–25 g.—and must be continued for at least 3 months if better results are to be achieved. Local treatment with 1–2% spray should also be included. Probably a P.A.S. "umbrella" will reduce the risk of spread or reactivation through operation or during pregnancy. It thus seems that P.A.S. may be regarded as the beginning of an answer to the problem of tuberculosis . . ."

Erdei A.: The Lancet, July 17, 1948 P 119

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